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Epidemiology of multimorbidity in NZ: A cross-sectional study using national-level hospital and pharmaceutical data

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TITLE: Epidemiology of multimorbidity in NZ: A cross-sectional study using national-level hospital and pharmaceutical data

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ABSTRACT

OBJECTIVES: To describe the prevalence of multimorbidity (presence of two or more long-term health conditions) in the New Zealand (NZ) population, and compare risk of health outcomes by multimorbidity status.

DESIGN: Cross-sectional analysis for prevalence of multimorbidity, with one-year prospective follow-up for health outcomes.

SETTING: NZ general population using national-level routine health data on hospital discharges and pharmaceutical dispensing.

PARTICIPANTS: All NZ adults (aged 18+, n=3,489,747) with an active National Health Index (NHI) number at the index date (1st Jan 2014).

OUTCOME MEASURES: Prevalence of multimorbidity was calculated using two data sources: routine hospital discharge data (ICD-10 coded diagnoses) using 61 conditions from the M3 multimorbidity index; and pharmaceutical dispensing records using 30 conditions from the P3 multimorbidity index.

METHODS: Prevalence of multimorbidity was calculated separately for the two data sources, stratified by age group, sex, ethnicity, and socioeconomic deprivation, and age-/sex-standardised to the total population. One-year risk of poor health outcomes (mortality, ambulatory sensitive hospitalisation (ASH), and overnight hospital admission) was compared by multimorbidity status using logistic regression adjusted for confounders.

RESULTS: Prevalence of multimorbidity was 7.9% based on hospital discharge data, and 27.9% using pharmaceutical dispensing data. Prevalence increased with age, with a clear socioeconomic gradient and differences in prevalence by ethnicity. Age/sex standardised one-year mortality risk was 2.7% for those with multimorbidity (defined on hospital discharge data), and 0.5% for those without multimorbidity (age/sex adjusted OR = 4.8, 95% CI 4.7, 5.0). Risk of ASH was also increased for those with multimorbidity (e.g. pharmaceutical discharge definition: age/sex-standardised risk 6.2%, compared to 1.8% for those without multimorbidity; age/sex-adjusted OR = 3.6, 95% CI 3.5, 3.6).

CONCLUSIONS: Multimorbidity is common in the NZ adult population, with disparities in who is affected. Providing for the needs of individuals with multimorbidity requires collaborative and coordinated work across the health sector.

KEYWORDS: multimorbidity, long-term conditions, chronic conditions, epidemiology

Strengths and limitations of the study

- This study uses national-level data for nearly 3.5 million New Zealand adults to provide robust estimates of the prevalence of multimorbidity.
- Multimorbidity was defined using existing methods to classify and code long-term health conditions, based on well-established data sources for hospital discharge and pharmaceutical dispensing data.
- Health outcome measures (mortality and hospital admission) were available for everyone in the study population.
- Due to the nature of the data sources, not all long-term health conditions could be measured: the estimates include only conditions recorded during a past hospital admission or those long-term conditions which can be treated by medication (and where medications are specific to treating a condition).
- Results may be only partially comparable with those studies from other countries that have used a primary-care based sampling frame or data source to estimate prevalence of multimorbidity.

INTRODUCTION

Health care delivery in secondary-care settings has typically been dominated by systems that focus on the treatment or management of a single disease,¹ such as cancer or diabetes, with less attention paid to other health conditions (which are typically conceptualised as comorbidities). Recently, more attention has been given towards the concept of multimorbidity, defined as the co-presence of two or more long-term health conditions,^{2,3} as a framework for viewing a patient's health needs from a more holistic management perspective.⁴⁻⁶ While such management is considered best practice in primary care settings, the quality of care provided in both secondary and primary care settings could be improved by encouraging a greater emphasis on this approach and considering the complex needs of patients with multimorbidity.⁷⁻⁹

This view of multimorbidity also requires consideration of the social and economic determinants of health that lie upstream of poor health generally.^{10,11} Long-term conditions are patterned by these determinants of health such as greater exposure to social, environmental or workplace risk factors, which in turn often pattern individual-level risk factors e.g. smoking, poor diet, lack of exercise, and poorer access to healthcare resources in the socioeconomically disadvantaged.

At an individual level, those with multimorbidity have poorer health outcomes, including increased risk stemming from polypharmacy, worse functional status, and lower quality of life.^{2,12,13} The implications of multimorbidity for health systems have been well described: expenditure on health care in high-income countries is dominated by the needs of those with multiple long-term conditions.^{5,14} Furthermore, while multimorbidity is not restricted to the elderly, it is more prevalent amongst older people.^{2,3} Therefore the healthcare demands and costs associated with multimorbidity will continue to rise as populations age,¹⁵ though the rising prevalence of multimorbidity does not appear to be solely driven by aging populations.¹⁶

There have been many prevalence studies of multimorbidity, as described in several systematic reviews.^{2,3,12,13} Studies have generally focussed on multimorbidity in specific populations (e.g. the elderly, or amongst hospitalised patients¹⁷); or examined the general population, either amongst registered populations using existing patient databases^{18,19} or using surveys of the general population;¹⁵ or have measured multimorbidity during primary care interactions.²⁰

A 2012 systematic review³ looked at variations in the prevalence of multimorbidity by country and research setting (e.g. primary health care patients, or across the general population.) Unsurprisingly, studies that sampled individual patients during primary care consultations have typically reported higher prevalence of multimorbidity compared to studies that used broader health-system based populations as the denominator (e.g. registered patients).³

This review made two major recommendations for studying multimorbidity: firstly, use a broad sample frame that matches the appropriate target population; and secondly, consider a reasonably comprehensive list of long-term conditions to capture the sheer variety of specific health needs that arise in long-term conditions (with a lower bound of 12 eligible conditions suggested as a minimum).³

In this paper we provide the first national-level report on the prevalence of multimorbidity in New Zealand (NZ) using hospital discharge and pharmaceutical dispensing data sources, including

describing the patterning of multimorbidity by major sociodemographic and socioeconomic groupings. We also examined subsequent health outcomes for those with multimorbidity, including mortality, ambulatory sensitive hospitalisations (ASH) and overnight admissions to hospital.

METHODS

Study design, setting and participants

This study is a cross-sectional prevalence study of multimorbidity across the NZ adult population, defined at 1st January 2014, using routinely collected, national level administrative health data for the preceding five years. Study size was determined by the total identified population at this index date.

The target study population was all NZ adults (aged 18+), operationally defined as individuals with an active National Health Index (NHI) number, based on active enrolment with a Primary Health Organisation (PHO) or recent interaction with the NZ health system in the year prior to the index date. Further details are given under data sources below. This target population covers the vast majority of New Zealanders (estimated around 94% across the entire population²¹).

Data sources

All data were sourced from the national collections as maintained by the NZ Ministry of Health.²¹ The population denominator and sociodemographic information were derived from the master NHI table. This source includes information on date of birth, sex, ethnicity, and place of residence, and can be linked to other national health data using the unique NHI identifier.

Information on long-term conditions was sourced from (1) the National Minimum Data Set (NMDS), which captures all publicly funded hospital discharges in NZ (and some privately funded), with diagnostic information relevant to the admission coded using ICD-10 codes; and (2) the Pharmaceutical collection, which includes all community-dispensed prescriptions across NZ, with medications coded using a modified version of the ATC classification system.^{22 23}

Long-term conditions were identified using the condition lists developed for the M3 index (for hospital discharge data,²⁴ based on all diagnoses recorded for discharges in the five-year lookback period) and the P3 index (for community pharmaceutical data (see Supplementary Material A), based on dispensings in a one year lookback period from the index date). Both indices were developed for considering mortality risk in population health analyses, with the individual conditions chosen based on chronicity, expected impact on mortality, and other long term impacts on health. The M3 index includes a total of 61 conditions, with the list of conditions intended to capture long-term conditions known to have some impact on mortality and/or morbidity. The P3 index includes a different, shorter list of 30 conditions, as the underlying pharmaceutical dispensing data can only capture conditions for which pharmaceutical treatment is possible. Furthermore, since some medications are used to treat multiple disparate conditions, it is not always possible to determine the precise condition or indication for a given medication. These medications with multiple common indications were thus excluded in the creation of the P3 index. Both of these indices are described in full detail elsewhere for the M3 index²⁴ and in Supplementary Material A for the P3 index, including full details of the exact codes included in their definitions for any condition.

Information on deaths during the follow-up period was drawn from the NZ Mortality Collection.

Variables

Multimorbidity was defined as having at least two conditions from the M3 or P3 condition list. Results are reported separately based on these two different data sources, as the conditions coded by each index do not fully align with each other. Supplementary results are reported using a higher threshold of at least three conditions to define multimorbidity. In addition to prevalence of multimorbidity, the numbers of identified conditions are reported using medians and interquartile range.

Prevalence estimates are reported stratified by several sociodemographic and socioeconomic factors. Age at the index date and sex were defined using information from the NHI master table (age grouped as 18-24, 25-34, 35-44, 45-54, 55-64, 65-74, 75-84, and 85+). Prevalence by broad ethnic groups (Māori, Pacific, Asian, European and Middle-Eastern/Latin American/African/Other [MELAA/Other]) is presented using a modified total ethnicity approach based on self-identified health as recorded in the NHI master table, in line with best practice in NZ health settings.²⁵ Total ethnicity reporting means that individuals who self-identify with more than one ethnic group were counted in both numerator and denominator for each of those groups: to allow some comparison in prevalence estimates, the European group was treated as a mutually exclusive group (i.e. containing individuals who only self-identified as NZ European or European). For regression analysis, ethnicity was prioritised so that individuals were only assigned to one group (in the order noted above) following standard practice.²⁵

Socioeconomic status was measured using the NZDep 2013 index,²⁶ an area based measure of socioeconomic deprivation produced from relevant information in the NZ census. This was matched to individual's health records based on their geocoded residential address in the NHI master record: in some cases this information was missing and hence an NZDep score could not be assigned to a person's record (missing data reported in Table 1).

We also considered several potential adverse outcomes from multimorbidity during the one-year follow-up period (1st January 2014 to 31 December 2014). Data was available for all participants across this period. All-cause mortality was considered alongside ambulatory sensitive hospitalisation (ASH admissions) and overnight hospital admissions. ASH admissions were defined based on a primary diagnosis in a specified list^{27 28} where the admission type was defined as either acute or arranged (i.e. excluding elective admissions, except in the case of dental procedures which are always coded as ASH regardless of admission type). Overnight hospital admissions were any admissions that included an overnight stay in hospital, with the exclusion of maternity related events (defined as any admission with a primary diagnosis ICD code starting with "O").

Statistical methods

Data coding and preparation was conducted in SAS 9.4 (SAS Institute, Cary, NC); all subsequent analyses were conducted using R 3.2 (R Foundation, Vienna, Austria).

Prevalence estimates are reported at the index date as crude percentages. For reporting of prevalence of multimorbidity stratified by other sociodemographic factors, we directly age- and sex-

standardised estimates for each sub-group to reflect the total adult NZ age/sex distribution (as calculated for the entire study population) using R's epitools package.²⁹

We also compared adverse outcomes (death, ambulatory sensitive hospitalisation [ASH], and overnight hospitalisation) within one year between individuals with and without multimorbidity, again in separate analyses with multimorbidity defined based on hospital diagnosis data or pharmaceutical dispensing data. Risks of outcomes within one year of the index date are initially presented as crude and age/sex-standardised risks for each outcome. We also report odds ratios (from binary logistic regression) comparing the odds of each outcome in models where we sequentially adjusted for confounder variables. The first model for each outcome presents unadjusted odds ratios; the second model adjusts for age group and sex; the third model additionally adjusts for prioritised ethnicity; and the fully-adjusted fourth model adds in adjustment for socioeconomic status using NZDep2013 (in quintiles as a categorical variable). Regression analysis was restricted to individuals with complete information on all covariates.

RESULTS

Table 1 gives the sociodemographic profile of the 3.49 million NZ adults in the study population at the index date (1st January 2014). Table 2 gives a list of the top 15 condition categories (as single conditions) identified across the population (i.e. not just amongst those with multimorbidity) for both the hospital diagnosis data (based on the M3 index categories) and the pharmaceutical dispensing data (based on the P3 index categories).

Prevalence estimates for multimorbidity at the index date are also presented in Table 1, for definitions based on the two data sources. Across the entire identified NZ adult population, 7.9% of the population were defined as having multimorbidity when using the hospital diagnosis data source; prevalence was considerably higher at 27.9% when using the pharmaceutical dispensing data source.

As expected, the prevalence of multimorbidity increased with age for both definitions, as also shown in Figure 1. Prevalence of multimorbidity was consistently higher based on pharmaceutical dispensing data compared to hospital admission data, with the difference widening in the older age groups. Multimorbidity based on hospital data was higher for males than females (8.6% and 7.4%, age standardised); while females had higher prevalence based on pharmaceutical dispensing (30.7% compared to 24.8% for males, age-standardised).

The crude prevalence of multimorbidity based on hospital data (Table 1, middle set of columns) was roughly similar across NZ European, Māori and Pacific populations (8.6 to 9.3%) and lower for Asian and MELAA/Other groups (4.6% and 4.7%). This was partially due to the NZ European group having an older population distribution: following age- and sex-standardisation, prevalence of multimorbidity was higher for Māori and Pacific ethnic groups (13.4% and 13.8% prevalence respectively) than for NZ European (7.6% prevalence), and the Asian and MELAA/Other groups (6.9 and 8.7% respectively) were also more in line with the NZ European prevalence. Figure 2 gives age-stratified estimates of multimorbidity by total ethnicity group, which shows early divergence by ethnicity in younger age groups but relatively similar trajectories of prevalence as age increases.

Table 1. Sociodemographic and socioeconomic description of study population at index date (1st Jan 2014)

Variable	Group	Total* n (column %)	Prevalence of Multimorbidity			
			Hospital Admissions n (%)	Standardised† %	Pharmaceuticals n (%)	Standardised† %
Total	Total	3,489,747 (100.0)	275,706 (7.9)	7.9	972,222 (27.9)	27.9
Age group	18-24	454,511 (13.0)	7,258 (1.6)	1.6	36,625 (8.1)	8.1
	25-34	605,263 (17.3)	12,334 (2.0)	2.0	69,041 (11.4)	11.4
	35-44	621,645 (17.8)	18,978 (3.1)	3.1	104,296 (16.8)	16.7
	45-54	646,669 (18.5)	33,987 (5.3)	5.3	160,862 (24.9)	24.9
	55-64	525,600 (15.1)	48,702 (9.3)	9.2	199,362 (37.9)	38.0
	65-74	366,866 (10.5)	62,869 (17.1)	17.1	201,807 (55.0)	55.0
	75-84	193,497 (5.5)	59,116 (30.6)	30.7	139,099 (71.9)	71.7
	85+	75,696 (2.2)	32,462 (42.9)	43.3	61,130 (80.8)	80.4
Sex	Female	1,807,908 (51.8)	135,615 (7.5)	7.3	561,921 (31.1)	30.7
	Male	1,681,839 (48.2)	140,091 (8.3)	8.6	410,301 (24.4)	24.8
Total Ethnicity‡	NZ European	2,292,963 (69.6)	197,471 (8.6)	7.6	725,030 (31.6)	29.0
	Māori	402,188 (12.2)	37,111 (9.2)	13.4	97,337 (24.2)	31.7
	Pacific	226,503 (6.9)	21,108 (9.3)	13.8	49,645 (21.9)	29.8
	Asian	360,349 (10.9)	16,726 (4.6)	6.9	68,926 (19.1)	24.3
	MELAA/Other	44,056 (1.3)	2,091 (4.7)	8.7	9,087 (20.6)	29.9
NZDep Quintile§	1	669,348 (19.2)	37,217 (5.6)	5.8	167,609 (25.0)	25.1
	2	653,071 (18.8)	44,000 (6.7)	6.7	173,294 (26.5)	26.3
	3	672,889 (19.3)	52,417 (7.8)	7.3	191,645 (28.5)	27.5
	4	737,521 (21.2)	66,749 (9.1)	8.7	222,336 (30.1)	29.6
	5	748,339 (21.5)	74,548 (10.0)	10.8	215,689 (28.8)	30.9

* Total column reports number of people in each sociodemographic category and their proportion of the total adult population at the index date.

† Standardised to age and sex profile of total study population (aged 18+; age groups as presented). All standardised confidence intervals were narrower than +/- 0.2%.

‡ People identifying with multiple ethnic groups are counted in each of these groups (and so total can sum to > 100%). n=192,910 individuals had no ethnicity recorded.

§ A total of 140,056 individuals had no NZDep quintile available (could not be matched to a valid NZDep area)

Table 2. Prevalence of top 15 individual condition categories (study group total N = 3,489,747) based on hospital admission data (top panel) and pharmaceutical dispensing data (bottom panel).

Condition (hospital data)	n	Prevalence (%)
Cardiac arrhythmia	76,469	2.2
Diabetes complicated	75,957	2.2
Hypertension uncomplicated	62,030	1.8
Metabolic disorder	57,937	1.7
Bowel disease inflammatory	56,335	1.6
Cardiac disease (other)	54,508	1.6
Chronic pulmonary disease	48,417	1.4
Coagulopathy and other blood disorders	43,329	1.2
Cerebrovascular disease	40,619	1.2
Myocardial infarction	36,811	1.1
Eye problem long term	36,266	1.0
Congestive heart failure	33,329	1.0
Angina	33,147	0.9
Major psychiatric disorder	32,687	0.9
Intestinal disorder	32,457	0.9

Condition (pharmaceutical data)	n	Prevalence (%)
Gastric acid disorder	514,562	14.7
CVD (Low Risk*)	495,386	14.2
Depression	418,512	12
Reactive airway disease	383,652	11
Anxiety and tension	318,563	9.1
CVD (Moderate Risk†)	302,317	8.7
Steroids responsive conditions	279,394	8.0
Diabetes	186,186	5.3
Hypothyroidism	113,098	3.2
Congestive heart failure	94,342	2.7
Anaemias	89,336	2.6
Psychotic illness	81,788	2.3
Epilepsy	77,040	2.2
Ischaemic heart disease/Angina	72,942	2.1
Anticoagulation	70,753	2.0

* Medication from one cardiovascular disease category

† Medication from two cardiovascular disease categories

Crude ethnic group differences in prevalence based on pharmaceutical dispensing (Table 1, right hand set of columns) were also confounded by age. Crude prevalence appeared relatively high in NZ European (31.6%) compared to the other ethnic groups (19.1-24.2%), but following age standardisation these differences were less pronounced (prevalence between 29 and 32% for all groups except Asian, with a standardised prevalence of 24.3%). Age-stratified ethnic patterns of multimorbidity based on pharmaceutical dispensing data are shown in Figure 2.

Multimorbidity was also more common amongst those in higher socioeconomic deprivation areas (based on NZDep2013), with standardised prevalence based on hospital diagnoses rising from 5.8% (least deprived quintile) to 10.8% (most deprived quintile); and for pharmaceutical based definitions from 25.1% (least deprived) to 30.9% (most deprived). These patterns were consistent across the age spectrum (Figure 3.)

Those with multimorbidity were at substantially higher risk of an adverse outcome in the year following the index date (mortality, ASH admission, non-maternity overnight admission). Table 3 gives the crude and age-/sex-standardised risk of each adverse outcome by multimorbidity status. Absolute risk was consistently higher across all outcomes for the multimorbidity group based on the hospital diagnosis definition than for the pharmaceutical dispensing. Figure 4 plots the age-/sex-standardised risks for each outcome according to multimorbidity status, based on the two data sources.

Table 4 shows the odds ratios for each adverse outcome by multimorbidity status, from logistic regression models. Unadjusted estimates (first row of Table 4) were largely confounded by age and sex: further adjustment for ethnicity and socioeconomic deprivation (NZDep) had minimal impact on estimates of comparisons by multimorbidity status. All results in the following text are from the fully adjusted model (bottom row of Table 4).

All three outcomes were substantially more common for those with multimorbidity than those without. While one-year mortality was just under 1% for the total adult population, those with multimorbidity had around a 3 to 5-fold higher risk of death (fully adjusted OR = 3.9, 95% CI 3.7, 4.0 for the pharmaceutical dispensing definition; and 4.6, 95% CI 4.5, 4.7 for the hospital diagnosis definition.) Fully adjusted odds ratios for the ASH and non-maternity hospital admission outcomes also indicated higher risk of hospitalisation for those with multimorbidity: odds ratios from models using the hospital diagnosis definition were again higher than the corresponding OR from the models using the pharmaceutical dispensing definition (Table 4).

Table 3. Crude and age/sex standardised risk of adverse outcomes within 12 months of index date.

Outcome	Total population (N=3,489,747)	Risk of outcome in following year			
		Hospital admissions definition		Pharmaceutical based definition	
		Multimorbid (N=275,706)	Not multimorbid (N=3,214,041)	Multimorbid (N=972,222)	Not multimorbid (N=2,517,525)
		n (crude %) [standardised %]*	n (crude %) [standardised %]*	n (crude %) [standardised %]*	n (crude %) [standardised %]*
Mortality	29,642 (0.8%)	17,536 (6.4%) [2.7%]	12,106 (0.4%) [0.5%]	25,131 (2.6%) [1.3%]	4,511 (0.2%) [0.4%]
ASH admission†	116,522 (3.3%)	45,509 (16.5%) [13.2%]	71,013 (2.2%) [2.4%]	78,347 (8.1%) [6.2%]	38,175 (1.5%) [1.8%]
Overnight admission‡	327,825 (9.4%)	88,285 (32.0%) [27.5%]	239,540 (7.5%) [7.9%]	183,406 (18.9%) [15.7%]	144,419 (5.7%) [6.5%]

Note. Confidence intervals are not printed: for crude risk, the margin of error on the 95% CI was ≤ 0.1%; for adjusted risk, ≤ 0.3%.

* Age- and sex-standardised to total study population profile.

† Ambulatory sensitive hospitalisation (ASH)

‡ Non-maternity admissions with at least an overnight stay.

Table 4. Odds ratios for increased risk of mortality/hospital admission with multimorbidity (according to hospital discharge or pharmaceutical based definition of multimorbidity) from unadjusted and adjusted logistic regression models.

Model†	Odds ratio (95% CI) for risk of outcome with multimorbidity*					
	Hospital discharge definition			Pharmaceutical dispensing definition		
	Mortality	ASH‡	Admission§	Mortality	ASH‡	Admission§
Unadjusted model	17.6 (17.2, 18.1)	8.4 (8.3, 8.5)	5.6 (5.6, 5.7)	14.7 (14.2, 15.2)	5.5 (5.5, 5.6)	3.7 (3.7, 3.7)
Adjusted age, sex	4.8 (4.7, 5.0)	4.9 (4.9, 5.0)	3.6 (3.5, 3.6)	4.0 (3.9, 4.2)	3.6 (3.6, 3.7)	2.6 (2.6, 2.7)
+ adjust ethnicity	4.7 (4.6, 4.8)	4.7 (4.6, 4.7)	3.5 (3.5, 3.5)	3.9 (3.8, 4.1)	3.6 (3.5, 3.6)	2.6 (2.6, 2.6)
+ adjust NZDep quintile	4.6 (4.5, 4.7)	4.6 (4.5, 4.6)	3.5 (3.4, 3.5)	3.9 (3.7, 4.0)	3.5 (3.5, 3.6)	2.6 (2.6, 2.6)

* Reference group is individuals without multimorbidity (i.e. either zero or only one long-term conditions identified)

† All models run on complete-case data only (n=3,288,646; total of n=201,101 missing ethnicity &/or NZDep)

‡ Ambulatory sensitive hospitalisation (ASH)

§ Non-maternity admissions with at least an overnight stay.

DISCUSSION

These results present the first nation-wide report of the prevalence of multimorbidity in nearly 3.5 million New Zealand adults. Over one-quarter of the adult population of NZ had multimorbidity when defined from pharmaceutical dispensing data (27.9%), although estimates were consistently lower when based on past hospital admission data (prevalence of 7.9% of all adults). Multimorbidity was more common amongst older people, those living in areas of higher socioeconomic deprivation, and in Māori and Pacific ethnic groups. People with multimorbidity were at higher risk of subsequent adverse outcomes (death and ASH or overnight hospitalisation) in the one-year follow-up period, even following adjustment for confounding from age and other sociodemographic factors.

The prevalence estimates for multimorbidity were generally consistent with international results: the pharmaceutical dispensing based estimate (27.9%) was firmly within estimates of prevalence from those studies that looked at a relatively broad range of age groups from early adulthood – these have typically ranged from 14-40%, with most studies reporting a prevalence between 20% and 30%.²³ Estimates from low and middle income countries have tended to be lower, supporting the hypothesis of epidemiological transition as an important driver in the prevalence of long-term disease,³⁰ though methodological variations may explain this difference. These results are concordant with recent studies in countries with similar population structures. Recent estimates from the United States put multimorbidity in the general population at around 22 to 26%, based on record linkage and survey data respectively.^{19 31} In Canada, survey estimates from the general population have recently been put as high as 59%³² or as low as 13%.³³

In Australia, the most recent national population estimates demonstrate a multimorbidity prevalence of around 33%³⁴ using primary-care attendance numerators and population denominators. A regional Australian study from New South Wales of adults aged 45 and over found prevalence of 36.1 to 37.4%, based on pharmaceutical claims data and survey data respectively; and a prevalence of 19.3% based on hospital discharge data.¹⁸ Restricting our own data to ages 45 and above returned a prevalence of 42.2% based on pharmaceutical dispensing data, and 13.1% based on hospital discharge data (not shown).

The key strengths of this analysis include the wide coverage of the NZ population, covering the vast majority of NZ adults engaged with the health system. The classification and coding of conditions in both the hospital discharge and pharmaceutical dispensing datasets also followed well-delineated methods²⁴ that are reproducible across time and different countries. These two data sources provide complementary definitions of what it means to have multimorbidity.

The key weaknesses are discussed below with respect to the utility of these two data sources. It is worth noting that neither the hospital nor pharmaceutical data source perfectly align with the prevalence of multimorbidity that could be determined from primary care interaction data; however, the national coverage and internal consistency of the hospitalisation and dispensing data sources used in this study improve the generalisability and utility of these data sources above what could be discovered from more locally-held primary care data sources, and the pharmaceutical dispensing data should provide a reasonable approximation for the prevalence of multimorbidity from primary care data. Unfortunately in NZ there is no national collation of primary care data from which the prevalence of multimorbidity can be calculated, and so primary-care level definitions of multimorbidity are not feasible at a national level.

The difference in prevalence estimates when using hospital admission and pharmaceutical dispensing data sources has implications for future research and planning. Using past hospital admission data identifies a smaller group of individuals with multimorbidity, but this group is at particularly elevated risk of subsequent poor outcomes (following adjustment for confounders like age and sex). This is highly suggestive of a more severe level of multimorbidity, which may be additionally captured in other analyses by accounting for recent hospital admission as

a separate risk factor variable. The appropriate choice of data source for considering multimorbidity based on routine data will ultimately depend on both data availability and the study question being addressed. The two systems also differ regarding the most commonly captured conditions: as one key example, mental health conditions were considerably more prominent when using the pharmaceutical definition than the hospitalisation definitions.

While a pharmaceutical dispensing definition sits closer to primary-care level definitions of multimorbidity, determination of long-term health conditions from pharmaceutical data is limited in that (a) some medications are used to treat different conditions, and (b) not all long-term health conditions might require or respond to pharmaceutical treatment. On top of this, cost-related factors that restrict the ability to access primary health care consultations and/or pay for prescriptions³⁵ mean that pharmaceutical dispensing based definitions may underestimate the prevalence of multimorbidity in socioeconomically deprived groups. Conversely, the number and breadth of diagnoses recorded on hospital discharge records are dependent on several factors, including the primary reason for the admission, requirements for reporting of health conditions in specific jurisdictions, and the quality of recording of information both by attending medical staff and clinical coders.^{36 37}

Other studies comparing different designs or data sources for estimating prevalence of multimorbidity have reported higher prevalence when the denominator comprises those currently receiving care or medication, compared to when denominators are based on registered patients or the general population.^{3 31} Recent studies from Quebec and Australia have suggested a 10% to 15% higher prevalence (respectively) when using a denominator based on primary care attendees rather than a general population denominator;^{32 34} and another study suggested higher prevalence when using health survey methods compared to examining electronic health records.³⁸ A recent Australian study that linked survey data (for ages 45 plus) with routine pharmaceutical and hospitalisation data returned comparable prevalence estimates between survey and pharmaceutical data sources (37.4 and 36.1%), which were both around 17 percentage points higher than prevalence estimated using hospital data (19.3%).¹⁸

There are important equity considerations that arise from the patterning of multimorbidity by age, ethnicity, and socioeconomic status, especially considered in conjunction with this group's increased risk of subsequent hospital admission or death within the one-year follow-up period. The higher prevalence of multimorbidity in the Māori and Pacific populations also raises issues of equity in health outcomes: as such, interventions in NZ that aim to prevent multimorbidity or improve outcomes for those with multimorbidity need to consider the equity impacts of such interventions.³⁹ While these prevalence results are specific to NZ, we expect that patterning of multimorbidity by sociodemographic profile and the adjusted estimates for increased risk of poor health outcomes with multimorbidity should be generalizable to other countries.

Conclusions

Multimorbidity is common amongst NZ adults, with older people, Māori and Pacific ethnic groups and the socioeconomically disadvantaged having higher prevalence (on both of the measures used). Pharmaceutical dispensing data should give a better proxy for the prevalence of multimorbidity that could be determined from primary-care level data sources compared to using past hospital admission diagnosis data, although these estimates may be subject to bias arising from differential access to healthcare and pharmaceuticals between different population groups (e.g. by ethnic groups).

Looking more broadly at the health system, these results support calls to consider the existence of multimorbidity in the design of health services, which requires a continued shift from management of individual diseases to care of the whole patient.^{8 9 40} The impact of an aging population (and hence higher numbers of people with multimorbidity) combined with the substantial costs of providing health care for people with multimorbidity^{5 14 15} will also present a major challenge to the sustainability of health care systems. This has important implications for both planning health services to improve management for those who are already unwell, but perhaps more importantly for justifying appropriate targeting of interventions aimed at preventing long-term conditions.⁷

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ACKNOWLEDGEMENTS:

Ethical approval was given by the University of Otago Human Ethics Committee (Health) at the start of the study (HD14/29). A poster showing results looking at the prevalence of multimorbidity in NZ in 2012 was presented at the World Congress of Epidemiology, Saitama, Japan, in August 2017.

We would like to thank Jane Zhang (MSc, University of Otago, Wellington) for her help in developing the SAS code to sort and count clinical conditions; and the Ministry of Health for supplying the data used in this study.

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COMPETING INTERESTS

JS, KM, EM, and DS report grants from Health Research Council of New Zealand during the conduct of the study.

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AUTHOR CONTRIBUTIONS

DS and JS conceived and obtained funding for the study.

JS designed and conducted the analyses, had full access to all of the data in this study and takes complete responsibility for the integrity of the data and the accuracy of the data analysis.

DS, KS, and EM contributed to the interpretation of the results.

JS drafted the manuscript.

All authors revised the manuscript for publication and approved the final version.

DATA SHARING

Data for this study were provided by the New Zealand Ministry of Health (reference number: 2017-0609) following ethical approval, and may be available to other researchers who meet data access requirements. Code for data processing and analysis is available from the first author (JS) on request.

FIGURE TITLES

Figure 1. Prevalence of multimorbidity (two or more conditions) by age group, according to hospital discharge diagnosis and pharmaceutical dispensing data sources

Figure 2. Prevalence of multimorbidity (two or more conditions) by age group and ethnicity, according to hospital discharge diagnosis and pharmaceutical dispensing data sources

Figure 3. Prevalence of multimorbidity (two or more conditions) by age group and NZDep quintile, according to hospital discharge diagnosis and pharmaceutical dispensing data sources

Figure 4. Age and sex standardised risk of mortality (left panel), ambulatory sensitive hospitalisation [ASH] admission (middle panel) and overnight non-maternity admission (right panel) within one year of index date, by multimorbidity status (defined based on hospital discharge diagnosis or pharmaceutical dispensing data)

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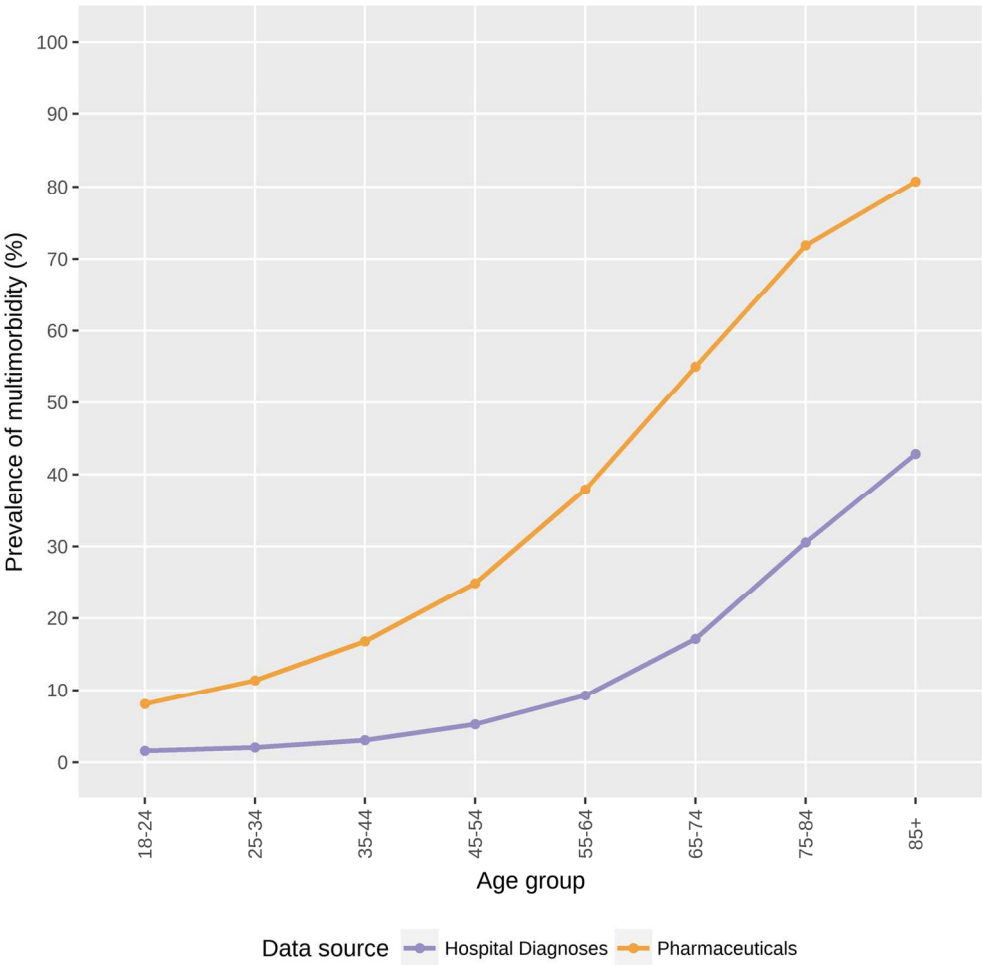
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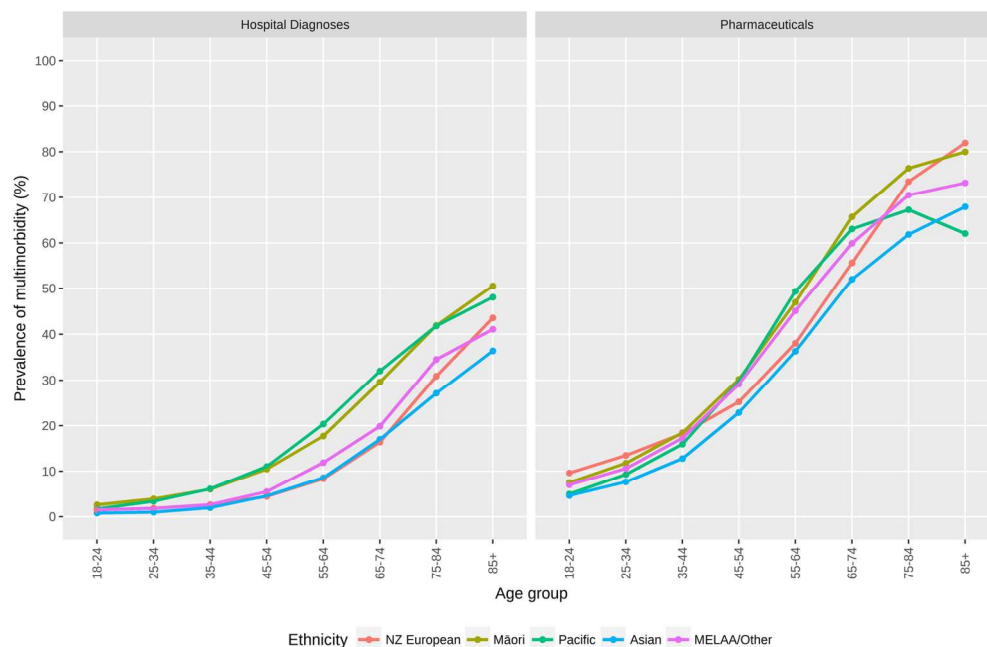
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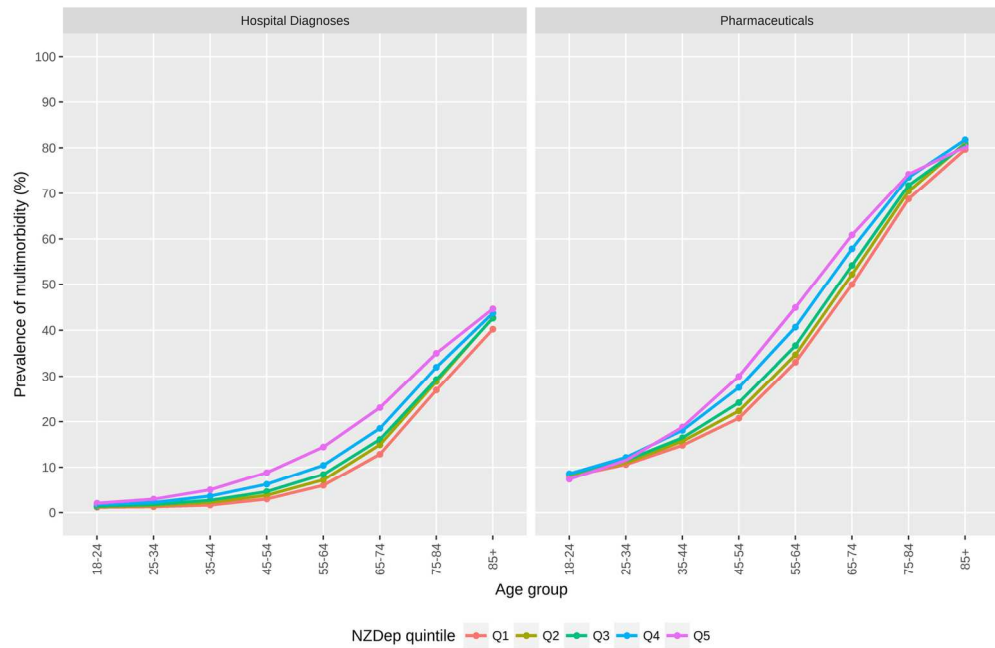
Prevalence of multimorbidity (two or more conditions) by age group, according to hospital discharge diagnosis and pharmaceutical dispensing data sources

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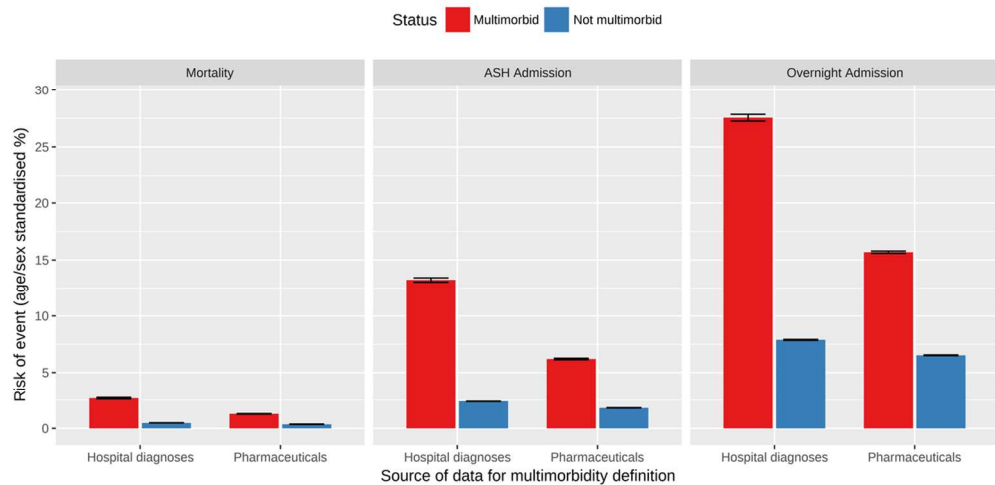
Prevalence of multimorbidity (two or more conditions) by age group and ethnicity, according to hospital discharge diagnosis and pharmaceutical dispensing data sources

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Prevalence of multimorbidity (two or more conditions) by age group and NZDep quintile, according to hospital discharge diagnosis and pharmaceutical dispensing data sources

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Age and sex standardised risk of mortality (left panel), ambulatory sensitive hospitalisation [ASH] admission (middle panel) and overnight non-maternity admission (right panel) within one year of index date, by multimorbidity status (defined based on hospital discharge diagnosis or pharmaceutical dispensing data)

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Supplementary Table A. Drug classes and medications included in the P3 index, with PHARMAC modified ATC codes and suggested ATC code classifications

Drug Class (details)	Medications included within class	PHARMAC Modified ATC codes*	ATC code groups**	ATC codes***
Anaemia	Hypoplastic and haemolytic; iron therapy; megaloblastic agents	13803, 40101, 40103, 40104	<u>B03A</u> <u>B03BA</u>	<u>A16AX03</u> B03AA03 B03BA01 <u>B03XA01</u> <u>B05XB01</u> <u>L03AA02</u> <u>L03AA03</u>
Anticoagulation	Heparin and Antagonist Preparations; Oral Anticoagulants	40704; 40707	<u>B01AA</u> <u>B01AB</u> <u>B01AE</u> <u>B01AF</u>	B01AA02 B01AA03 B01AB01 B01AB04 B01AB05 B01AE07 B01AF01 <u>V03AB14</u>
Anxiety and tension	Anxiolytics (Benzodiazepine, Barbiturate); sedatives and hypnotics	222501; 222801	<u>N05B</u> <u>N05CA</u> <u>N05CC</u> <u>N05CD</u> <u>N05CF</u>	N05BA01 N05BA02 N05BA04 N05BA06 N05BA08 N05BA12 N05BC01 N05BE01 N05CA24 N05CC01 N05CC01 N05CD02 N05CD03 N05CD05 N05CD06 N05CD07 N05CD08 N05CD11 N05CF01

Arrhythmias	Anti-arrhythmics	71301	<u>C01B</u>	<u>C01AA05</u> C01BA01 C01BA02 C01BA03 C01BB01 C01BB02 C01BB03 C01BC03 C01BC04 C01BD01
Congestive heart failure (CHF)	Loop diuretics	73101	<u>C03CA</u>	C03CA01 C03CA02
Dementia	Donepezil, Rivastigmine	223201	<u>N06D</u>	N06DA02 N06DA03
Depression	Cyclic, MAOI, SSRI and other antidepressants	220501,220504,220505,220509,220507, 221001, 221002, 221007	<u>N06A</u>	N06AA01 N06AA02 N06AA04 N06AA06 N06AA09 N06AA10 N06AA10 N06AA12 N06AA16 N06AA17 N06AA21 N06AB03 N06AB03 N06AB04 N06AB05 N06AB06 N06AB06 N06AB10 N06AF03 N06AF04 N06AG02 N06AX03 N06AX06 N06AX11 N06AX11 N06AX16 N06AX16

Gastric acid disorder	H2 blockers; proton pump inhibitors; other antiulcerants; antacids	10102, 10104, 11001, 11003, 11002, 11007, 11010, 11013	<u>A02A</u> <u>A02B</u>	A02AA05 A02AB01 A02AC01 A02AF02 A02BA01 A02BA02 A02BA03 A02BA04 A02BB01 A02BC01 A02BC02 A02BC03 A02BD01 A02BD05 A02BD08 A02BX01 A02BX02 A02BX03 A02BX05 A02BX12 A02BX13
Hepatitis B/C	Interferon/Ribavirin combinations	161905, 162201		<u>J05AF05</u> <u>J05AF08</u> <u>J05AF10</u> <u>L03AB04</u> <u>L03AB05</u> <u>L03AB10</u> <u>L03AB11</u> <u>L03AB60</u>

Osteoporosis/Paget's	Alendronate; Etidronate; Calcium supplementation	13801, 190802, 190804, 190806	<u>H05BA</u> <u>M05BA</u> <u>M05BB</u>	<u>A12AA</u> <u>G03XC01</u> <u>H05AA02</u> H05BA01 M05BA01 M05BA03 M05BA04 M05BA07 M05BA08 M05BB01 M05BB02 M05BB03 M05BB04 M05BB07 M05BB08 <u>V03AG01</u>
Pancreatic insufficiency	Pancreatic exocrine enzyme replacements	12201	<u>A05AA</u>	A05AA01 A05AA02 <u>A09AA02</u>
Parkinson's disease	Antiparkinsonian agents (dopamine agonists, specified anticholinergics)	221904, 221901, 220101	<u>N04</u>	<u>N01AX03</u> <u>N01BB01</u> N04AA02 N04BA01 N04BA01 N04BB01 N04BC01 N04BC02 N04BC04 N04BC04 N04BC05 N04BC05 N04BC07 N04BD01 N04BX01 N04BX02

Psychotic illness	Antipsychotics (oral and depot)	222204, 222201, 222208	N05AA01 N05AA02 N05AB02 N05AB02 N05AB06 N05AC01 N05AC02 N05AC04 N05AD01 N05AD01 N05AD08 N05AE04 N05AF01 N05AF04 N05AF05 N05AG01 N05AG02 N05AH01 N05AH02 N05AH03 N05AH04 N05AL01 N05AL05 N05AN01 N05AX08 N05AX12 N05AX13
Pulmonary hypertension, PVD	Endothelin receptor antagonists; Phosphodiesterase Type 5 inhibitors; Prostacyclin analogues; vasodilators	74005, 74007, 74009, 74001	<u>C01DX16</u> <u>C02DB02</u> <u>C02DC01</u> <u>C02KX01</u> <u>C02KX02</u> <u>C04AC02</u> <u>C04AD03</u> <u>C04AX01</u> <u>V03AB22</u>

Reactive airway disease	Inhaled bronchodilators and corticosteroids; anticholinergic agents; mast cell stabilisers; Leukotriene inhibitors; respiratory devices	283001, 283010, 283401, 283410, 281001, 282404, 282402, 284001, 284302, 284502, 285302	<u>R03</u>	<u>C01CA26</u> <u>N06BC01</u> R03AB03 R03AC02 R03AC03 R03AC04 R03AC06 R03AC12 R03AC13 R03AC18 R03BA01 R03BA02 R03BA05 R03BB01 R03BC01 R03BC03 R03CC02 R03CC03 R03CC04 R03CC05 R03CC12 R03DA04 R03DA02 R03DA05
Rheumatoid arthritis	Antirheumatoid agents; TNF inhibitors	190701, 190702	<u>M01C</u>	<u>L04AA13</u> <u>L04AB01</u> M01CB01 M01CB03 M01CB04 M01CC01 <u>M02AB01</u>
Steroids-responsive conditions	Glucocorticoids (systemic corticosteroids)	140701	<u>H02AA</u> <u>H02AB</u>	<u>H01AA01</u> H02AA02 H02AB01 H02AB02 H02AB04 H02AB06 H02AB07 H02AB08 H02AB09 H02AB10

Transplant/ Auto-immune disorders	Immunosuppressants	250701, 250706		<u>L01XE10</u> <u>L04AA06</u> <u>L04AA10</u> <u>L04AD01</u> <u>L04AD02</u> <u>L04AX01</u>
Tuberculosis	Antitubercular agents	161601	<u>J04A</u>	<u>J01MA09</u> J04AA01 J04AB01 J04AB02 J04AB04 J04AB30 J04AC01 J04AD01 J04AD03 J04AK01 J04AK02 J04AM02 <u>J04BA01</u> <u>J04BA02</u>
CVD medication categories:				
Antiplatelet	Antiplatelet agents; coagulation check strips****	40701		<u>B01AB10</u> <u>B01AC04</u> <u>B01AC06</u> <u>B01AC07</u> <u>B01AC22</u> <u>B01AC24</u>
Hyperlipidaemia	Lipid lowering agents	41301, 41304, 41302, 41303, 41308, 73201, 73202, 73203, 73205, 73208	<u>C10AB</u> <u>C10AC</u>	C10AB01 C10AB02 C10AB04 C10AC01 C10AC02 <u>C10AD02</u> <u>C10AD06</u> <u>C10AD52</u> <u>C10AX02</u> <u>C10AX06</u> <u>C10AX09</u>

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2			<u>C02A</u>	C02AB01
3				C02AB02
4				C02AC01
5			<u>C02C</u>	C02CA01
6				C02CA04
7				C02CC02
8			<u>C03A</u>	C03AA01
9				C03AA04
10				C03AA07
11				C03AA08
12			<u>C03B</u>	C03AB01
13				C03BA04
14				C03BA08
15				C03BA11
16			<u>C03D</u>	C03DA01
17				C03DB01
18				C03DB01
19				C03DB02
20			<u>C03EA</u>	C03EA13
21	Ischemic heart	Beta blockers; calcium channel blockers;	70101, 70701, 70702, 70703, 71601,	<u>C04AB01</u>
22	disease/Hypertension	ACE inhibitors; Angiotensin II inhibitors;	71901, 72201, 72202, 72801, 73107,	<u>C04AX02</u>
23		Thiazides; Potassium-sparing agents;	73104, 73110, 70401, 70705	
24		combination antihypertensives; diuretics		<u>C07AA01-08</u>
25		and other hypertensives (Clonidine,		C07AA01
26		Hydralazine)		C07AA02
27				C07AA03
28				C07AA05
29				C07AA06
30				C07AA07
31				C07AA12
32			<u>C07AB02-08</u>	C07AB02
33				C07AB03
34				C07AB04
35				C07AB07
36				C07AB08
37			<u>C07AG</u>	C07AG01
38				C07AG02
39			<u>C08CA</u>	C08CA01
40				C08CA02
41				C08CA03
42				C08CA05
43				<u>C08DA01</u>
44				<u>C08DB01</u>
45				<u>C08EX02</u>
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				C09AA02
				C09AA03
				C09AA04
				C09AA06
				C09AA07
				C09AA08
				C09AA10
			<u>C09CA</u>	C09CA01
				C09CA06

* PHARMAC’s modified ATC codes, as available in the core data source and used in classification of indices.

** Suggested mapping to ATC code groups.

***Suggested specific ATC codes based on medications discovered in current NZ Pharmaceutical data for this analysis. Bolded/underlined items are single-code suggestions that do not fall under the groupings in the preceding column.

**** Some or all items coded in the PHARMAC-modified ATC coding system have no corresponding item in the WHO’s ATC coding system.

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page # / note
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4-5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants (b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	5 n/a
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5
Bias	9	Describe any efforts to address potential sources of bias	(discussion)
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses	6-7 n/a p.6 n/a none

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	n/a (cross-sectional)
		(c) Consider use of a flow diagram	Not included (one-step selection)
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	
		(b) Indicate number of participants with missing data for each variable of interest	Table 1, Table 4 (footnotes to each)
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	P6. For prospective element
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	p. 8, Table 3
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	n/a
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	n/a
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	p. 7-10, all tables and figures.
		(b) Report category boundaries when continuous variables were categorized	Table 1, Figs 1-3
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Absolute risk on p. 7-10, Table 4
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	n/a (none performed)
Discussion			
Key results	18	Summarise key results with reference to study objectives	p. 13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	p.13-14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	p.13-14
Generalisability	21	Discuss the generalisability (external validity) of the study results	p. 14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	p3 and online statement

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Epidemiology of multimorbidity in New Zealand: A cross-sectional study using national-level hospital and pharmaceutical data

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Keywords:	multimorbidity, long-term conditions, chronic conditions, EPIDEMIOLOGY

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TITLE: Epidemiology of multimorbidity in New Zealand: A cross-sectional study using national-level hospital and pharmaceutical data

AUTHORS: James Stanley¹, Kelly Semper¹, Elinor Millar¹, Diana Sarfati¹

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ABSTRACT

OBJECTIVES: To describe the prevalence of multimorbidity (presence of two or more long-term health conditions) in the New Zealand (NZ) population, and compare risk of health outcomes by multimorbidity status.

DESIGN: Cross-sectional analysis for prevalence of multimorbidity, with one-year prospective follow-up for health outcomes.

SETTING: NZ general population using national-level routine health data on hospital discharges and pharmaceutical dispensing.

PARTICIPANTS: All NZ adults (aged 18+, n=3,489,747) with an active National Health Index (NHI) number at the index date (1st Jan 2014).

OUTCOME MEASURES: Prevalence of multimorbidity was calculated using two data sources: routine hospital discharge data (ICD-10 coded diagnoses) using 61 conditions from the M3 multimorbidity index; and pharmaceutical dispensing records using 30 conditions from the P3 multimorbidity index.

METHODS: Prevalence of multimorbidity was calculated separately for the two data sources, stratified by age group, sex, ethnicity, and socioeconomic deprivation, and age-/sex-standardised to the total population. One-year risk of poor health outcomes (mortality, ambulatory sensitive hospitalisation (ASH), and overnight hospital admission) was compared by multimorbidity status using logistic regression adjusted for confounders.

RESULTS: Prevalence of multimorbidity was 7.9% based on hospital discharge data, and 27.9% using pharmaceutical dispensing data. Prevalence increased with age, with a clear socioeconomic gradient and differences in prevalence by ethnicity. Age/sex standardised one-year mortality risk was 2.7% for those with multimorbidity (defined on hospital discharge data), and 0.5% for those without multimorbidity (age/sex adjusted OR = 4.8, 95% CI 4.7, 5.0). Risk of ASH was also increased for those with multimorbidity (e.g. pharmaceutical discharge definition: age/sex-standardised risk 6.2%, compared to 1.8% for those without multimorbidity; age/sex-adjusted OR = 3.6, 95% CI 3.5, 3.6).

CONCLUSIONS: Multimorbidity is common in the NZ adult population, with disparities in who is affected. Providing for the needs of individuals with multimorbidity requires collaborative and coordinated work across the health sector.

KEYWORDS: multimorbidity, long-term conditions, chronic conditions, epidemiology

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Strengths and limitations of the study

- This study uses national-level data for nearly 3.5 million New Zealand adults to provide robust estimates of the prevalence of multimorbidity.
- Multimorbidity was defined using existing methods to classify and code long-term health conditions, based on well-established data sources for hospital discharge and pharmaceutical dispensing data.
- Health outcome measures (mortality and hospital admission) were available for everyone in the study population.
- Due to the nature of the data sources, not all long-term health conditions could be measured: the estimates include only conditions recorded during a past hospital admission or those long-term conditions which can be treated by medication (and where medications are specific to treating a condition).
- Results may be only partially comparable with those studies from other countries that have used a primary-care based sampling frame or data source to estimate prevalence of multimorbidity.

INTRODUCTION

Health care delivery in secondary-care settings has typically been dominated by systems that focus on the treatment or management of a single disease,¹ such as cancer or diabetes, with less attention paid to other health conditions (which are typically conceptualised as comorbidities). Recently, more attention has been given towards the concept of multimorbidity, defined as the co-presence of two or more long-term health conditions,^{2,3} as a framework for viewing a patient's health needs from a more holistic management perspective.⁴⁻⁶ While such management is considered best practice in primary care settings, the quality of care provided in both secondary and primary care settings could be improved by encouraging a greater emphasis on this approach and considering the complex needs of patients with multimorbidity.⁷⁻⁹

This view of multimorbidity also requires consideration of the social and economic determinants of health that lie upstream of poor health generally.^{10,11} Long-term conditions are patterned by these determinants of health such as greater exposure to social, environmental or workplace risk factors, which in turn often pattern individual-level risk factors e.g. smoking, poor diet, lack of exercise, and poorer access to healthcare resources in the socioeconomically disadvantaged.

At an individual level, those with multimorbidity have poorer health outcomes, including increased risk stemming from polypharmacy, worse functional status, and lower quality of life.^{2,12,13} The implications of multimorbidity for health systems have been well described: expenditure on health care in high-income countries is dominated by the needs of those with multiple long-term conditions.^{5,14} Furthermore, while multimorbidity is not restricted to the elderly, it is more prevalent amongst older people.^{2,3} Therefore the healthcare demands and costs associated with multimorbidity will continue to rise as populations age,¹⁵ though the rising prevalence of multimorbidity does not appear to be solely driven by aging populations.¹⁶

There have been many prevalence studies of multimorbidity, as described in several systematic reviews.^{2,3,12,13} Studies have generally focussed on multimorbidity in specific populations (e.g. the elderly^{17,18}, or amongst hospitalised patients¹⁸); or examined the general population, either amongst registered populations using existing patient databases^{19,20} or using surveys of the general population;¹⁵ or have measured multimorbidity during primary care interactions.²¹

A 2012 systematic review³ looked at variations in the prevalence of multimorbidity by country and research setting (e.g. primary health care patients, or across the general population.) Unsurprisingly, studies that sampled individual patients during primary care consultations have typically reported higher prevalence of multimorbidity compared to studies that used broader health-system based populations as the denominator (e.g. registered patients).³

This review made two major recommendations for studying multimorbidity: firstly, use a broad sample frame that matches the appropriate target population; and secondly, consider a reasonably comprehensive list of long-term conditions to capture the sheer variety of specific health needs that arise in long-term conditions (with a lower bound of 12 eligible conditions suggested as a minimum).³

Our primary objective was to describe the prevalence of multimorbidity for the general adult population in New Zealand (NZ), defining multimorbidity status using past hospital discharge and

pharmaceutical dispensing records. To examine health inequities, we also analysed the patterning of multimorbidity by major sociodemographic and socioeconomic groupings. As a secondary objective, we examined subsequent health outcomes for those with multimorbidity, including mortality, ambulatory sensitive hospitalisations (ASH) and overnight admissions to hospital.

METHODS

Study design, setting and participants

This study is a cross-sectional prevalence study of multimorbidity across the NZ adult population, defined at 1st January 2014, using routinely collected, national level administrative health data. We also examined subsequent health outcomes for the year following this index date. Study size was determined by the total identified population at this index date.

The target study population was all NZ adults (aged 18+), operationally defined as individuals with an active National Health Index (NHI) number, based on active enrolment with a Primary Health Organisation (PHO) or recent interaction with the NZ health system in the year prior to the index date (n=3,489,747). No additional inclusion or exclusion criteria were applied. Further details are given under data sources below. This target population covers the vast majority of New Zealanders (it is estimated that around 94% of the entire population are enrolled with a PHO²², and so the actual coverage should be in excess of 94% when including additional individuals who meet the recent-interaction criteria for an active NHI number).

Patient and Public Involvement

Patients and members of the public were not involved in the design or conduct of this study.

Data sources

All data were sourced from the national collections as maintained by the NZ Ministry of Health.²² The population denominator and sociodemographic information were derived from the master NHI table. This source includes information on date of birth, sex, ethnicity, and place of residence, and can be linked to other national health data using the unique NHI identifier.

Information on long-term conditions was sourced from (1) the National Minimum Data Set (NMDS), which captures all publicly funded hospital discharges in NZ (and some privately funded), with diagnostic information relevant to the admission coded using ICD-10 codes; and (2) the Pharmaceutical collection, which includes all community-dispensed prescriptions across NZ, with medications coded using a modified version of the ATC classification system.^{23 24}

Long-term conditions were identified using the condition lists developed for the M3 index (for hospital discharge data,²⁵ based on all diagnoses recorded for discharges in the five-year lookback period) and the P3 index (for community pharmaceutical data (see Supplementary Table A), based on dispensings in a one year lookback period from the index date). Both indices were developed for considering mortality risk in population health analyses, with the individual conditions chosen based on chronicity, expected impact on mortality, and other long term impacts on health. The M3 index includes a total of 61 conditions, with the list of conditions intended to capture long-term conditions known to have some impact on mortality and/or morbidity. The P3 index includes a different,

shorter list of 30 conditions, as the underlying pharmaceutical dispensing data can only capture conditions for which pharmaceutical treatment is possible. Furthermore, since some medications are used to treat multiple disparate conditions, it is not always possible to determine the precise condition or indication for a given medication. These medications with multiple common indications were thus excluded in the creation of the P3 index. Both of these indices are described in full detail elsewhere for the M3 index²⁵ and in Supplementary Table A for the P3 index, including full details of the exact codes included in their definitions for any condition.

Information on deaths during the follow-up period was drawn from the NZ Mortality Collection.

Variables

Multimorbidity was defined as having at least two conditions from the M3 or P3 condition list. Results are reported separately based on these two different data sources, as the conditions coded by each index do not fully align with each other. Supplementary results are reported using a higher threshold of at least three conditions to define multimorbidity. In addition to prevalence of multimorbidity, the numbers of identified conditions are reported using medians and interquartile range.

Prevalence estimates are reported stratified by several sociodemographic and socioeconomic factors. Age at the index date and sex were defined using information from the NHI master table (age grouped as 18-24, 25-34, 35-44, 45-54, 55-64, 65-74, 75-84, and 85+). Prevalence by broad ethnic groups (Māori, Pacific, Asian, European and Middle-Eastern/Latin American/African/Other [MELAA/Other]) is presented using a modified total ethnicity approach based on self-identified health as recorded in the NHI master table, in line with best practice in NZ health settings.²⁶ Total ethnicity reporting means that individuals who self-identify with more than one ethnic group were counted in both numerator and denominator for each of those groups: to allow some comparison in prevalence estimates, the European group was treated as a mutually exclusive group (i.e. containing individuals who only self-identified as NZ European or European). For regression analysis, ethnicity was prioritised so that individuals were only assigned to one group (in the order noted above) following standard practice.²⁶

Socioeconomic status was measured using the NZDep 2013 index,²⁷ an area based measure of socioeconomic deprivation produced from relevant information in the NZ census. This was matched to individual's health records based on their geocoded residential address in the NHI master record: in some cases this information was missing and hence an NZDep score could not be assigned to a person's record (missing data reported in Table 1).

We also considered several potential adverse outcomes from multimorbidity during the one-year follow-up period (1st January 2014 to 31 December 2014). Data was available for all participants across this period. All-cause mortality was considered alongside ambulatory sensitive hospitalisation (ASH admissions) and overnight hospital admissions. ASH admissions were defined based on a primary diagnosis in a specified list^{28 29} where the admission type was defined as either acute or arranged (i.e. excluding elective admissions, except in the case of dental procedures which are always coded as ASH regardless of admission type). Overnight hospital admissions were any admissions that included an overnight stay in hospital, with the exclusion of maternity related events (defined as any admission with a primary diagnosis ICD code starting with "O").

Statistical methods

Data coding and preparation was conducted in SAS 9.4 (SAS Institute, Cary, NC); all subsequent analyses were conducted using R 3.2 (R Foundation, Vienna, Austria).

Prevalence estimates for the NZ adult population are reported at the index date as crude percentages. For reporting of prevalence of multimorbidity stratified by other sociodemographic factors, we directly age- and sex-standardised estimates for each sub-group to reflect the total adult NZ age/sex distribution (as calculated for the entire study population) using R's epitools package.³⁰ Prevalence for the total NZ adult population is also reported following direct age-standardisation to the World Health Organisation (WHO) world standard.³¹

We also compared adverse outcomes (death, ambulatory sensitive hospitalisation [ASH], and overnight hospitalisation) within one year between individuals with and without multimorbidity, again in separate analyses with multimorbidity defined based on hospital diagnosis data or pharmaceutical dispensing data. Risks of outcomes within one year of the index date are initially presented as crude and age/sex-standardised risks for each outcome. We also report odds ratios (from binary logistic regression) comparing the odds of each outcome in models where we sequentially adjusted for confounder variables. The first model for each outcome presents unadjusted odds ratios; the second model adjusts for age group and sex; the third model additionally adjusts for prioritised ethnicity; and the fully-adjusted fourth model adds in adjustment for socioeconomic status using NZDep2013 (in quintiles as a categorical variable). Regression analysis was restricted to individuals with complete information on all covariates (complete case analysis).

Sensitivity analysis

To address the impact of missing covariate data (5.8% of individuals missing ethnicity and/or NZDep quintile), we used multiple imputation to examine whether the associations measured in the main analysis could have been biased due to exclusion of individuals with missing data (complete case analysis). Five imputation datasets were created using chained equations³² (using the mice package³³ in R). These datasets imputed missing values for ethnicity and NZDep quintile (as polynomial variables) based on all other variables in the analytical model including exposure variables and outcome variables (multimorbidity status, age group, sex, ethnicity, NZDep quintile, and all outcome variables). The imputation models also included auxiliary information on each person's District Health Board of residence (the 20 administrative divisions of the public health system in NZ, which provides additional information on sub-national distribution of people by ethnicity and socioeconomic deprivation). Further details on this analysis and underlying assumptions are given with Supplementary Table B.

RESULTS

Table 1 gives the sociodemographic profile of the 3.49 million NZ adults in the study population at the index date (1st January 2014). Table 2 gives a list of the top 15 condition categories (as single conditions) identified across the population (i.e. not just amongst those with multimorbidity) for both the hospital diagnosis data (based on the M3 index categories) and the pharmaceutical dispensing data (based on the P3 index categories).

Prevalence estimates for multimorbidity in the adult population at the index date are also presented in Table 1, for definitions of multimorbidity drawing from each of the two data sources (past hospitalisation discharge records and past pharmaceutical dispensing). Across the entire identified NZ adult population, 7.9% of the population were defined as having multimorbidity when using the hospital diagnosis data source; prevalence was considerably higher at 27.9% when using the pharmaceutical dispensing data source. When age-standardised to the WHO standard age structure, these prevalences were 6% and 23% respectively.

As expected, the prevalence of multimorbidity increased with age for both definitions, as also shown in Figure 1. Prevalence of multimorbidity was consistently higher based on pharmaceutical dispensing data compared to hospital admission data, with the difference widening in the older age groups. Multimorbidity based on hospital data was higher for males than females (8.6% and 7.4%, age standardised); while females had higher prevalence based on pharmaceutical dispensing (30.7% compared to 24.8% for males, age-standardised). Differences between males and females in patterns of multimorbidity by age are shown in Figure 2: the higher prevalence using hospital discharge data amongst males becomes manifest by the 55-64 age group, while higher prevalence for females compared to males based on pharmaceutical dispensing data was apparent across all age groups.

The crude prevalence of multimorbidity based on hospital data (Table 1, middle set of columns) was roughly similar across NZ European, Māori and Pacific populations (8.6 to 9.3%) and lower for Asian and MELAA/Other groups (4.6% and 4.7%). This was partially due to the NZ European group having an older population distribution: following age- and sex-standardisation, prevalence of multimorbidity was higher for Māori and Pacific ethnic groups (13.4% and 13.8% prevalence respectively) than for NZ European (7.6% prevalence), and the Asian and MELAA/Other groups (6.9 and 8.7% respectively) were also more in line with the NZ European prevalence. Figure 3 gives age-stratified estimates of multimorbidity by total ethnicity group, which shows early divergence by ethnicity in younger age groups but relatively similar trajectories of prevalence as age increases.

Table 1. Sociodemographic and socioeconomic description of study population at index date (1st Jan 2014)

Variable	Group	Total* n (column %)	Prevalence of Multimorbidity			
			Hospital Admissions n (%)	Standardised† %	Pharmaceuticals n (%)	Standardised† %
Total	Total	3,489,747 (100.0)	275,706 (7.9)	7.9	972,222 (27.9)	27.9
Age group	18-24	454,511 (13.0)	7,258 (1.6)	1.6	36,625 (8.1)	8.1
	25-34	605,263 (17.3)	12,334 (2.0)	2.0	69,041 (11.4)	11.4
	35-44	621,645 (17.8)	18,978 (3.1)	3.1	104,296 (16.8)	16.7
	45-54	646,669 (18.5)	33,987 (5.3)	5.3	160,862 (24.9)	24.9
	55-64	525,600 (15.1)	48,702 (9.3)	9.2	199,362 (37.9)	38.0
	65-74	366,866 (10.5)	62,869 (17.1)	17.1	201,807 (55.0)	55.0
	75-84	193,497 (5.5)	59,116 (30.6)	30.7	139,099 (71.9)	71.7
	85+	75,696 (2.2)	32,462 (42.9)	43.3	61,130 (80.8)	80.4
Sex	Female	1,807,908 (51.8)	135,615 (7.5)	7.3	561,921 (31.1)	30.7
	Male	1,681,839 (48.2)	140,091 (8.3)	8.6	410,301 (24.4)	24.8
Total Ethnicity‡	NZ European	2,292,963 (69.6)	197,471 (8.6)	7.6	725,030 (31.6)	29.0
	Māori	402,188 (12.2)	37,111 (9.2)	13.4	97,337 (24.2)	31.7
	Pacific	226,503 (6.9)	21,108 (9.3)	13.8	49,645 (21.9)	29.8
	Asian	360,349 (10.9)	16,726 (4.6)	6.9	68,926 (19.1)	24.3
	MELAA/Other	44,056 (1.3)	2,091 (4.7)	8.7	9,087 (20.6)	29.9
NZDep Quintile§	1	669,348 (19.2)	37,217 (5.6)	5.8	167,609 (25.0)	25.1
	2	653,071 (18.8)	44,000 (6.7)	6.7	173,294 (26.5)	26.3
	3	672,889 (19.3)	52,417 (7.8)	7.3	191,645 (28.5)	27.5
	4	737,521 (21.2)	66,749 (9.1)	8.7	222,336 (30.1)	29.6
	5	748,339 (21.5)	74,548 (10.0)	10.8	215,689 (28.8)	30.9

* Total column reports number of people in each sociodemographic category and their proportion of the total adult population at the index date.

† Standardised to age and sex profile of total study population (aged 18+; age groups as presented). All standardised confidence intervals were narrower than +/- 0.2%.

‡ People identifying with multiple ethnic groups are counted in each of these groups (and so total can sum to > 100%). n=192,910 individuals had no ethnicity recorded.

§ A total of 140,056 individuals had no NZDep quintile available (could not be matched to a valid NZDep area)

Table 2. Prevalence of top 15 individual condition categories (study group total N = 3,489,747) based on hospital admission data (top panel) and pharmaceutical dispensing data (bottom panel).

Condition (hospital data)	n	Prevalence (%)
Cardiac arrhythmia	76,469	2.2
Diabetes complicated	75,957	2.2
Hypertension uncomplicated	62,030	1.8
Metabolic disorder	57,937	1.7
Bowel disease inflammatory	56,335	1.6
Cardiac disease (other)	54,508	1.6
Chronic pulmonary disease	48,417	1.4
Coagulopathy and other blood disorders	43,329	1.2
Cerebrovascular disease	40,619	1.2
Myocardial infarction	36,811	1.1
Eye problem long term	36,266	1.0
Congestive heart failure	33,329	1.0
Angina	33,147	0.9
Major psychiatric disorder	32,687	0.9
Intestinal disorder	32,457	0.9

Condition (pharmaceutical data)	n	Prevalence (%)
Gastric acid disorder	514,562	14.7
CVD (Low Risk*)	495,386	14.2
Depression	418,512	12
Reactive airway disease	383,652	11
Anxiety and tension	318,563	9.1
CVD (Moderate Risk†)	302,317	8.7
Steroids responsive conditions	279,394	8.0
Diabetes	186,186	5.3
Hypothyroidism	113,098	3.2
Congestive heart failure	94,342	2.7
Anaemias	89,336	2.6
Psychotic illness	81,788	2.3
Epilepsy	77,040	2.2
Ischaemic heart disease/Angina	72,942	2.1
Anticoagulation	70,753	2.0

* Medication from one cardiovascular disease category

† Medication from two cardiovascular disease categories

Crude ethnic group differences in prevalence based on pharmaceutical dispensing (Table 1, right hand set of columns) were also confounded by age. Crude prevalence appeared relatively high in NZ European (31.6%) compared to the other ethnic groups (19.1-24.2%), but following age standardisation these differences were less pronounced (prevalence between 29 and 32% for all groups except Asian, with a standardised prevalence of 24.3%). Age-stratified ethnic patterns of multimorbidity based on pharmaceutical dispensing data are shown in Figure 3.

Multimorbidity was also more common amongst those in higher socioeconomic deprivation areas (based on NZDep2013), with standardised prevalence based on hospital diagnoses rising from 5.8% (least deprived quintile) to 10.8% (most deprived quintile); and for pharmaceutical based definitions from 25.1% (least deprived) to 30.9% (most deprived). These patterns were consistent across the age spectrum (Figure 4.)

Those with multimorbidity were at substantially higher risk of an adverse outcome in the year following the index date (mortality, ASH admission, non-maternity overnight admission). Table 3 gives the crude and age-/sex-standardised risk of each adverse outcome by multimorbidity status. Absolute risk was consistently higher across all outcomes for the multimorbidity group based on the hospital diagnosis definition than for the pharmaceutical dispensing. Figure 5 plots the age-/sex-standardised risks for each outcome according to multimorbidity status, based on the two data sources.

Table 4 shows the odds ratios for each adverse outcome by multimorbidity status, from logistic regression models. Unadjusted estimates (first row of Table 4) were largely confounded by age and sex: further adjustment for ethnicity and socioeconomic deprivation (NZDep) had minimal impact on estimates of comparisons by multimorbidity status. All results in the following text are from the complete-case analysis for the fully adjusted model (bottom row of Table 4).

All three outcomes were substantially more common for those with multimorbidity than those without. While one-year mortality was just under 1% for the total adult population, those with multimorbidity had around a 3 to 5-fold higher risk of death (fully adjusted OR = 3.9, 95% CI 3.7, 4.0 for the pharmaceutical dispensing definition; and 4.6, 95% CI 4.5, 4.7 for the hospital diagnosis definition.) Fully adjusted odds ratios for the ASH and non-maternity hospital admission outcomes also indicated higher risk of hospitalisation for those with multimorbidity: odds ratios from models using the hospital diagnosis definition were again higher than the corresponding OR from the models using the pharmaceutical dispensing definition (Table 4).

The analyses looking at health outcomes were repeated following multiple imputation for missing data on ethnicity and socioeconomic deprivation (5.8% of cases). As shown in Supplementary Table B, adjusted estimates following imputation were not substantially different from the estimates from complete-case analysis. For example, for the analysis of mortality risk according to multimorbidity defined on hospital-discharge data: complete case analysis OR = 4.6 (95% CI 4.5, 4.7); multiple-imputation pooled OR = 4.7 (95% CI 4.6, 4.8). Other estimates from the imputed data analysis were also of similar magnitude to the main results in Table 4 (Supplementary Table B).

Table 3. Crude and age/sex standardised risk of adverse outcomes within 12 months of index date.

Outcome	Total population (N=3,489,747)	Risk of outcome in following year			
		Hospital admissions definition		Pharmaceutical based definition	
		Multimorbid (N=275,706)	Not multimorbid (N=3,214,041)	Multimorbid (N=972,222)	Not multimorbid (N=2,517,525)
		n (crude %) [standardised %]*	n (crude %) [standardised %]*	n (crude %) [standardised %]*	n (crude %) [standardised %]*
Mortality	29,642 (0.8%)	17,536 (6.4%) [2.7%]	12,106 (0.4%) [0.5%]	25,131 (2.6%) [1.3%]	4,511 (0.2%) [0.4%]
ASH admission†	116,522 (3.3%)	45,509 (16.5%) [13.2%]	71,013 (2.2%) [2.4%]	78,347 (8.1%) [6.2%]	38,175 (1.5%) [1.8%]
Overnight admission‡	327,825 (9.4%)	88,285 (32.0%) [27.5%]	239,540 (7.5%) [7.9%]	183,406 (18.9%) [15.7%]	144,419 (5.7%) [6.5%]

Note. Confidence intervals are not printed: for crude risk, the margin of error on the 95% CI was $\leq 0.1\%$; for adjusted risk, $\leq 0.3\%$.

* Age- and sex-standardised to total study population profile.

† Ambulatory sensitive hospitalisation (ASH)

‡ Non-maternity admissions with at least an overnight stay.

Table 4. Odds ratios for increased risk of mortality/hospital admission with multimorbidity (according to hospital discharge or pharmaceutical based definition of multimorbidity) from unadjusted and adjusted logistic regression models.

Model†	Odds ratio (95% CI) for risk of outcome with multimorbidity*					
	Hospital discharge definition			Pharmaceutical dispensing definition		
	Mortality	ASH‡	Admission§	Mortality	ASH‡	Admission§
Unadjusted model	17.6 (17.2, 18.1)	8.4 (8.3, 8.5)	5.6 (5.6, 5.7)	14.7 (14.2, 15.2)	5.5 (5.5, 5.6)	3.7 (3.7, 3.7)
Adjusted age, sex	4.8 (4.7, 5.0)	4.9 (4.9, 5.0)	3.6 (3.5, 3.6)	4.0 (3.9, 4.2)	3.6 (3.6, 3.7)	2.6 (2.6, 2.7)
+ adjust ethnicity	4.7 (4.6, 4.8)	4.7 (4.6, 4.7)	3.5 (3.5, 3.5)	3.9 (3.8, 4.1)	3.6 (3.5, 3.6)	2.6 (2.6, 2.6)
+ adjust NZDep quintile	4.6 (4.5, 4.7)	4.6 (4.5, 4.6)	3.5 (3.4, 3.5)	3.9 (3.7, 4.0)	3.5 (3.5, 3.6)	2.6 (2.6, 2.6)

* Reference group is individuals without multimorbidity (i.e. either zero or only one long-term conditions identified)

† All models run on complete-case data only (n=3,288,646; total of n=201,101 missing ethnicity &/or NZDep)

‡ Ambulatory sensitive hospitalisation (ASH)

§ Non-maternity admissions with at least an overnight stay.

DISCUSSION

These results present the first nation-wide report of the prevalence of multimorbidity in nearly 3.5 million New Zealand adults. Over one-quarter of the adult population of NZ had multimorbidity when defined from pharmaceutical dispensing data (27.9%), although estimates were consistently lower when based on past hospital admission data (prevalence of 7.9% of all adults). Multimorbidity was more common amongst older people, those living in areas of higher socioeconomic deprivation, and in Māori and Pacific ethnic groups. People with multimorbidity were at higher risk of subsequent adverse outcomes (death and ASH or overnight hospitalisation) in the one-year follow-up period, even following adjustment for confounding from age and other sociodemographic factors.

The prevalence estimates for multimorbidity were generally consistent with international results: the pharmaceutical dispensing based estimate (27.9%) was firmly within estimates of prevalence from those studies that looked at a relatively broad range of age groups from early adulthood – these have typically ranged from 14-40%, with most studies reporting a prevalence between 20% and 30%.²³ Estimates from low and middle income countries have tended to be lower, supporting the hypothesis of epidemiological transition as an important driver in the prevalence of long-term disease,³⁴ though methodological variations may explain this difference. These results are concordant with recent studies in countries with similar population structures. Recent estimates from the United States put multimorbidity in the general population at around 22 to 26%, based on record linkage and survey data respectively.^{20 35} In Canada, survey estimates from the general population have recently been put as high as 59%³⁶ or as low as 13%.³⁷ For future comparisons, the prevalence estimates following age standardisation to the WHO age standard were 6% and 23% respectively for definitions based on the hospital discharge and pharmaceutical dispensing data sources.

In Australia, the most recent national population estimates demonstrate a multimorbidity prevalence of around 33%³⁸ using primary-care attendance numerators and population denominators. A regional Australian study from New South Wales of adults aged 45 and over found prevalence of 36.1 to 37.4%, based on pharmaceutical claims data and survey data respectively; and a prevalence of 19.3% based on hospital discharge data.¹⁹ Restricting our own data to ages 45 and above returned a prevalence of 42.2% based on pharmaceutical dispensing data, and 13.1% based on hospital discharge data (not shown).

One result of interest for the regression analyses was that there was little change in the magnitude of the associations (between multimorbidity and each health outcome) when adjusting for ethnicity and socioeconomic deprivation (on top of adjustment for age group and sex). This is suggestive that ethnicity and socioeconomic deprivation were not substantial confounders of the association between multimorbidity and subsequent outcomes: it is important to note that the results of the fully-adjusted regression models (not presented) indicated that these two factors were independently associated with the outcome, such that there was still evidence for ethnic inequities and a socioeconomic gradient in outcomes.

The key strengths of this analysis include the wide coverage of the NZ population, covering the vast majority of NZ adults engaged with the health system. The classification and coding of conditions in both the hospital discharge and pharmaceutical dispensing datasets also followed well-delineated methods²⁵ that are reproducible across time and different countries. These two data sources provide complementary definitions of what it means to have multimorbidity.

The key weaknesses are discussed below with respect to the utility of these two data sources. It is worth noting that neither the hospital nor pharmaceutical data source perfectly align with the prevalence of multimorbidity that could be determined from primary care interaction data; however, the national coverage and internal consistency of the hospitalisation and dispensing data sources used in this study improve the generalisability and utility of these data sources above what could be discovered from more locally-held primary care data sources, and the pharmaceutical

1 dispensing data should provide a reasonable approximation for the prevalence of multimorbidity from primary care
2 data. Unfortunately in NZ there is no national collation of primary care data from which the prevalence of
3 multimorbidity can be calculated, and so primary-care level definitions of multimorbidity are not feasible at a
4 national level.

5
6 A second issue arising from the data sources was missing data for the regression models (which was 5.8% of total
7 group missing ethnicity and/or deprivation measure). While there is no uniform consensus on when the amount of
8 missing cases in a regression analysis is likely to bias results, in methodological work the threshold for considering
9 the impact of missing data typically starts at around 10% of cases having missing data (e.g. ^{39 40}). Furthermore,
10 regression models for complete cases (i.e. those with all covariate data available) that adjust for covariates
11 potentially related to missingness (including exposure and confounder variables) have been demonstrated to be
12 unbiased in comparison to more complex analytical methods (e.g. ⁴¹). Our sensitivity analysis using multiple
13 imputation suggested that the adjusted complete-case logistic regression results presented in Table 4 were not
14 biased compared to using multiple imputation.

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17 The final issue is that the data sources used cover adults defined as being engaged with the NZ health system (either
18 through enrolment with a PHO, estimated to cover around 94% of the population; or having used publicly funded
19 health services in the year prior to the index date). It is only possible to speculate about those individuals who are
20 not covered in these data sources: however, we do know that they will not have been in contact with health services
21 in the period used to define multimorbidity, and hence would not be able to meet the operational definitions of
22 multimorbidity used in this study (as these are based on hospital admissions and pharmaceutical dispensing).

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25 The difference in prevalence estimates when using hospital admission and pharmaceutical dispensing data sources
26 has implications for future research and planning. Using past hospital admission data identifies a smaller group of
27 individuals with multimorbidity, but this group is at particularly elevated risk of subsequent poor outcomes
28 (following adjustment for confounders like age and sex). This is highly suggestive of a more severe level of
29 multimorbidity, which may be additionally captured in other analyses by accounting for recent hospital admission as
30 a separate risk factor variable. The appropriate choice of data source for considering multimorbidity based on
31 routine data will ultimately depend on both data availability and the study question being addressed. The two
32 systems also differ regarding the most commonly captured conditions: as one key example, mental health conditions
33 were considerably more prominent when using the pharmaceutical definition than the hospitalisation definitions. As
34 an additional note, the number of long-term conditions used in defining multimorbidity is known to impact on the
35 measured prevalence: a systematic review recommended a minimum of 12 conditions to facilitate comparable
36 estimates across studies. ³ The conditions included in the current study were selected as reflecting long-term
37 conditions with some impact on subsequent serious health outcomes²⁵, and as such the definition of multimorbidity
38 used here strikes a balance between the number of conditions considered and the severity of their impact.

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41 While a pharmaceutical dispensing definition sits closer to primary-care level definitions of multimorbidity,
42 determination of long-term health conditions from pharmaceutical data is limited in that (a) some medications are
43 used to treat different conditions, and (b) not all long-term health conditions might require or respond to
44 pharmaceutical treatment. On top of this, cost-related factors that restrict the ability to access primary health care
45 consultations and/or pay for prescriptions ⁴² mean that pharmaceutical dispensing based definitions may
46 underestimate the prevalence of multimorbidity in socioeconomically deprived groups. Conversely, the number and
47 breadth of diagnoses recorded on hospital discharge records are dependent on several factors, including the primary
48 reason for the admission, requirements for reporting of health conditions in specific jurisdictions, and the quality of
49 recording of information both by attending medical staff and clinical coders. ^{43 44}

50
51 Other studies comparing different designs or data sources for estimating prevalence of multimorbidity have
52 reported higher prevalence when the denominator comprises those currently receiving care or medication,
53 compared to when denominators are based on registered patients or the general population. ^{3 35} Recent studies

from Quebec and Australia have suggested a 10% to 15% higher prevalence (respectively) when using a denominator based on primary care attendees rather than a general population denominator;^{36 38} and another study suggested higher prevalence when using health survey methods compared to examining electronic health records.⁴⁵ A recent Australian study that linked survey data (for ages 45 plus) with routine pharmaceutical and hospitalisation data returned comparable prevalence estimates between survey and pharmaceutical data sources (37.4 and 36.1%), which were both around 17 percentage points higher than prevalence estimated using hospital data (19.3%).¹⁹

There are important equity considerations that arise from the patterning of multimorbidity by age, ethnicity, and socioeconomic status, especially considered in conjunction with this group's increased risk of subsequent hospital admission or death within the one-year follow-up period. The higher prevalence of multimorbidity in the Māori and Pacific populations also raises issues of equity in health outcomes: as such, interventions in NZ that aim to prevent multimorbidity or improve outcomes for those with multimorbidity need to consider the equity impacts of such interventions.⁴⁶ While these prevalence results are specific to NZ, we expect that patterning of multimorbidity by sociodemographic profile and the adjusted estimates for increased risk of poor health outcomes with multimorbidity should be generalizable to other countries.

Conclusions

Multimorbidity is common amongst NZ adults, with older people, Māori and Pacific ethnic groups and the socioeconomically disadvantaged having higher prevalence (on both of the measures used). Pharmaceutical dispensing data should give a better proxy for the prevalence of multimorbidity that could be determined from primary-care level data sources compared to using past hospital admission diagnosis data, although these estimates may be subject to bias arising from differential access to healthcare and pharmaceuticals between different population groups (e.g. by ethnic groups).

Looking more broadly at the health system, these results support calls to consider the existence of multimorbidity in the design of health services, which requires a continued shift from management of individual diseases to care of the whole patient.^{8 9 47} The impact of an aging population (and hence higher numbers of people with multimorbidity) combined with the substantial costs of providing health care for people with multimorbidity^{5 14 15} will also present a major challenge to the sustainability of health care systems. This has important implications for both planning health services to improve management for those who are already unwell, but perhaps more importantly for justifying appropriate targeting of interventions aimed at preventing long-term conditions.⁷

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COMPETING INTERESTS

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AUTHOR CONTRIBUTIONS

DS and JS conceived and obtained funding for the study.

JS designed and conducted the analyses, had full access to all of the data in this study and takes complete responsibility for the integrity of the data and the accuracy of the data analysis.

DS, KS, and EM contributed to the interpretation of the results.

JS drafted the manuscript.

All authors revised the manuscript for publication and approved the final version.

DATA SHARING

Data for this study were provided by the New Zealand Ministry of Health (reference number: 2017-0609) following ethical approval, and may be available to other researchers who meet data access requirements. Code for data processing and analysis is available from the first author (JS) on request.

FIGURE TITLES

Figure 1. Prevalence of multimorbidity (two or more conditions) by age group, according to hospital discharge diagnosis and pharmaceutical dispensing data sources

Figure 2. Prevalence of multimorbidity (two or more conditions) by age group and sex, according to hospital discharge diagnosis and pharmaceutical dispensing data sources

Figure 3. Prevalence of multimorbidity (two or more conditions) by age group and ethnicity, according to hospital discharge diagnosis and pharmaceutical dispensing data sources

Figure 4. Prevalence of multimorbidity (two or more conditions) by age group and NZDep quintile, according to hospital discharge diagnosis and pharmaceutical dispensing data sources

Figure 5. Age and sex standardised risk of mortality (left panel), ambulatory sensitive hospitalisation [ASH] admission (middle panel) and overnight non-maternity admission (right panel) within one year of index date, by multimorbidity status (defined based on hospital discharge diagnosis or pharmaceutical dispensing data)

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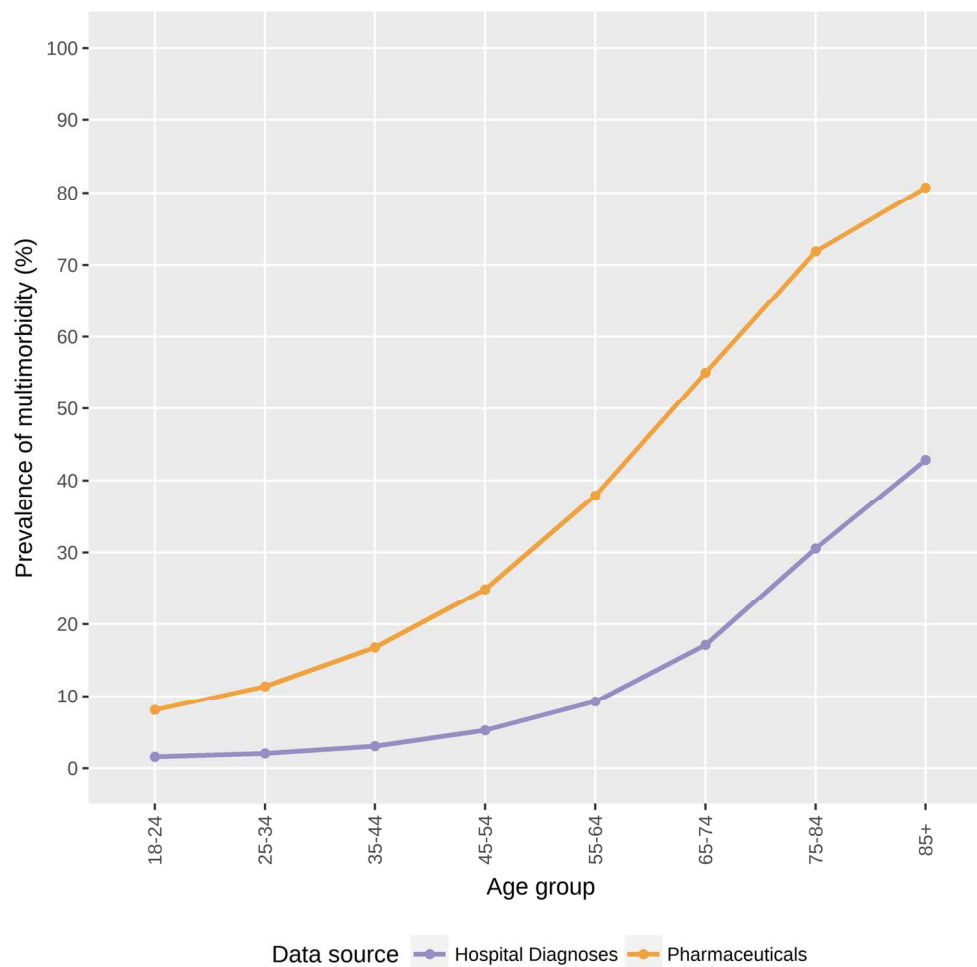


Figure 1: Prevalence of multimorbidity (two or more conditions) by age group, according to hospital discharge diagnosis and pharmaceutical dispensing data sources

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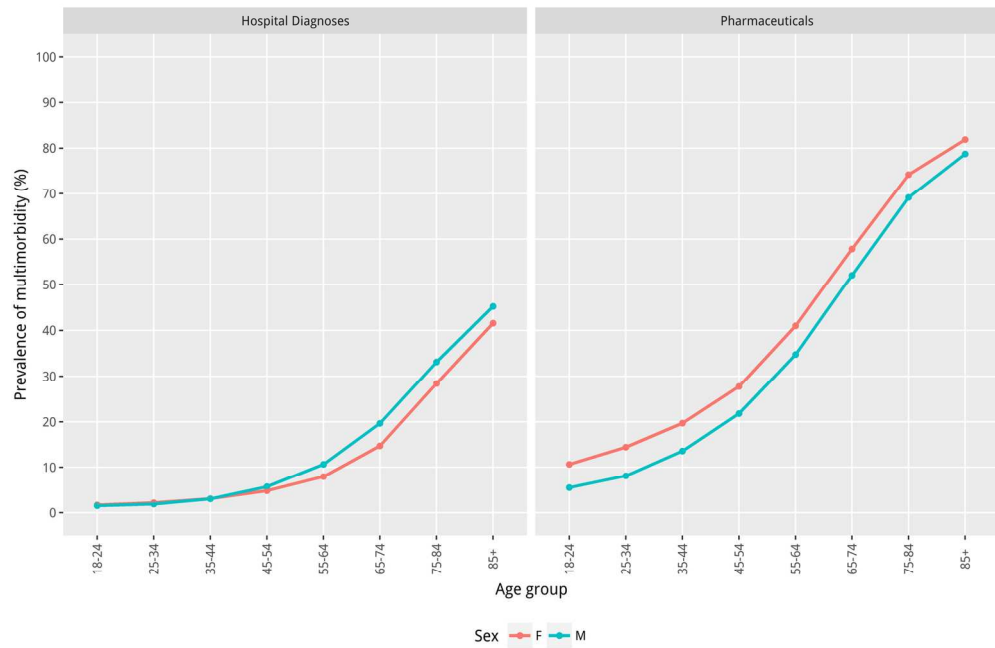


Figure 2: Prevalence of multimorbidity (two or more conditions) by age group and sex, according to hospital discharge diagnosis and pharmaceutical dispensing data sources

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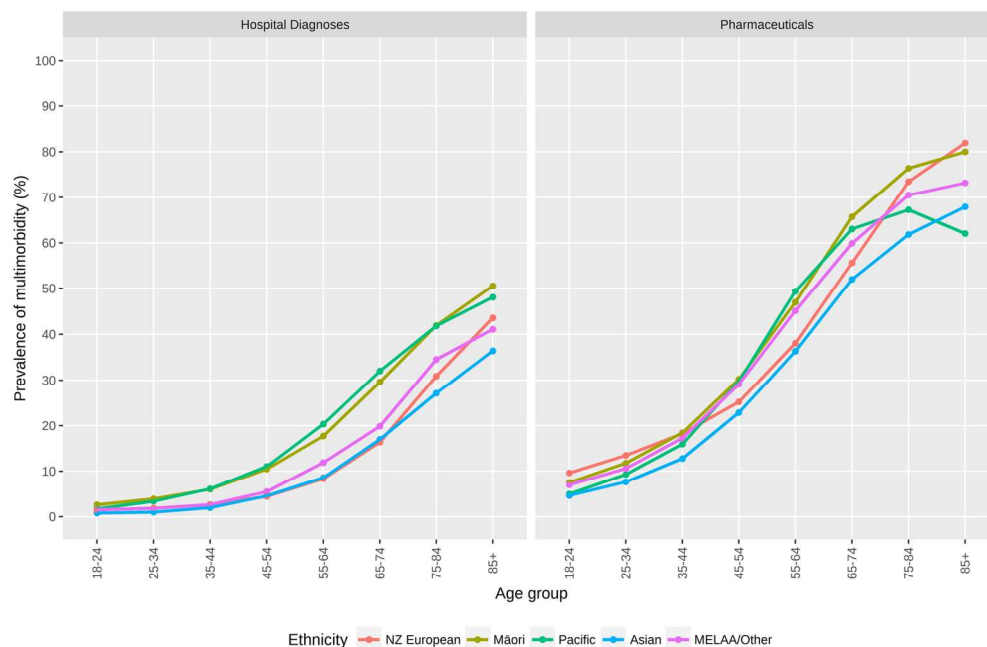


Figure 3: Prevalence of multimorbidity (two or more conditions) by age group and ethnicity, according to hospital discharge diagnosis and pharmaceutical dispensing data sources

152x101mm (300 x 300 DPI)

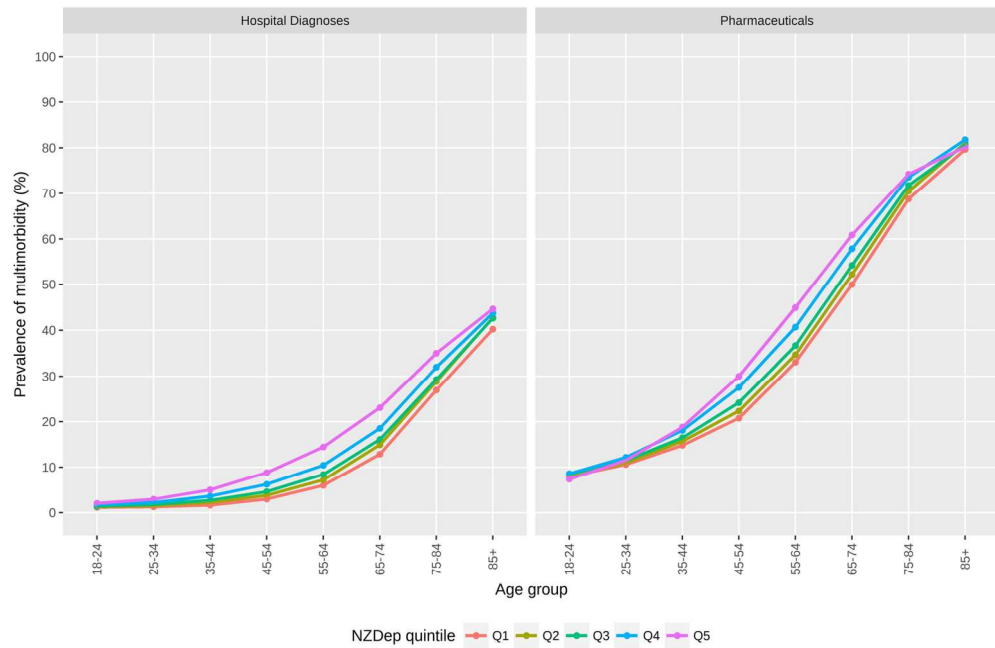


Figure 4: Prevalence of multimorbidity (two or more conditions) by age group and NZDep quintile, according to hospital discharge diagnosis and pharmaceutical dispensing data sources

152x101mm (300 x 300 DPI)

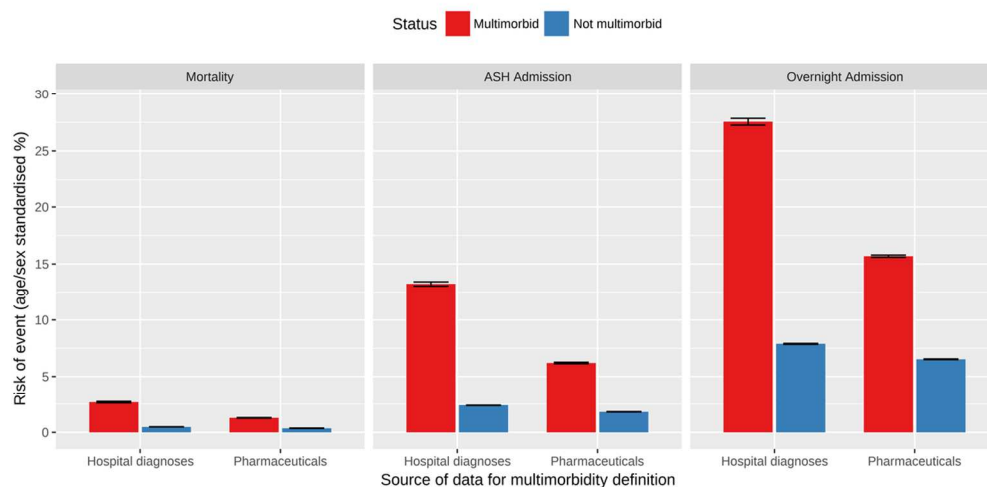


Figure 5: Age and sex standardised risk of mortality (left panel), ambulatory sensitive hospitalisation [ASH] admission (middle panel) and overnight non-maternity admission (right panel) within one year of index date, by multimorbidity status (defined based on hospital discharge diagnosis or pharmaceutical dispensing data)

114x57mm (300 x 300 DPI)

Supplementary Table A. Drug classes and medications included in the P3 index, with PHARMAC modified ATC codes and suggested ATC code classifications

[illegible]

1				<u>C01B</u>	<u>C01AA05</u>
2					C01BA01
3					C01BA02
4					C01BA03
5	Arrhythmias	Anti-arrhythmics	71301		C01BB01
6					C01BB02
7					C01BB03
8					C01BC03
9					C01BC04
10					C01BD01
11	Congestive heart failure (CHF)	Loop diuretics	73101	<u>C03CA</u>	C03CA01
12					C03CA02
13	Dementia	Donepezil, Rivastigmine	223201	<u>N06D</u>	N06DA02
14					N06DA03
15				<u>N06A</u>	N06AA01
16					N06AA02
17					N06AA04
18					N06AA06
19					N06AA09
20					N06AA10
21					N06AA10
22					N06AA12
23					N06AA16
24					N06AA17
25					N06AA21
26					N06AB03
27					N06AB03
28	Depression	Cyclic, MAOI, SSRI and other antidepressants	220501,220504,220505,220509,220507,221001, 221002, 221007		N06AB04
29					N06AB05
30					N06AB06
31					N06AB06
32					N06AB10
33					N06AF03
34					N06AF04
35					N06AG02
36					N06AX03
37					N06AX06
38					N06AX11
39					N06AX11
40					N06AX16
41					N06AX16

1					<i>Insulin products</i>
2					<i>(prefix)</i>
3				<u>A10A</u>	A10A
4					<i>Other products:</i>
5				<u>A10B</u>	A10BA02
6					A10BB01
7					A10BB02
8					A10BB03
9	Diabetes	Insulin; oral hypoglycaemics; Insulin/glucose testing equipment****	11311,11301,11305,11307,11309,11303, 11312, 11507,11501,11509,11512, 11515,11504,420603		A10BB05
10					A10BB07
11					A10BB09
12					A10BF01
13					A10BG02
14					A10BG03
15					A16AB06
16				<u>H01BA</u>	H01BA02
17					<u>H04AA01</u>
18					<u>V03AH01</u>
19				<u>N03A</u>	N03AA02
20					N03AA03
21					N03AB02
22					N03AD01
23					N03AE01
24					N03AF01
25					N03AF02
26					N03AG01
27	Epilepsy	Anticonvulsants	220701, 220702, 220703		N03AG04
28					N03AX03
29					N03AX09
30					N03AX11
31					N03AX12
32					N03AX14
33					N03AX17
34					N03AX18
35					<u>N05BA09</u>
36					<u>N05CC05</u>

Gastric acid disorder	H2 blockers; proton pump inhibitors; other antiulcerants; antacids	10102, 10104, 11001, 11003, 11002, 11007, 11010, 11013	<u>A02A</u> <u>A02B</u>	A02AA05 A02AB01 A02AC01 A02AF02 A02BA01 A02BA02 A02BA03 A02BA04 A02BB01 A02BC01 A02BC02 A02BC03 A02BD01 A02BD05 A02BD08 A02BX01 A02BX02 A02BX03 A02BX05 A02BX12 A02BX13
Hepatitis B/C	Interferon/Ribavirin combinations	161905, 162201		<u>J05AF05</u> <u>J05AF08</u> <u>J05AF10</u> <u>L03AB04</u> <u>L03AB05</u> <u>L03AB10</u> <u>L03AB11</u> <u>L03AB60</u>

		<u>J05AG</u>
		<u>J05AR</u>
ents	141401	<u>H03A</u>
	73401	<u>C01DA</u>
ritional supplements****	420201, 420202, 420203, 420204, 420401, 420632, 420631, 420604, 420605	<u>N03C</u>

Osteoporosis/Paget's	Alendronate; Etidronate; Calcium supplementation	13801, 190802, 190804, 190806	<u>H05BA</u> <u>M05BA</u> <u>M05BB</u>	<u>A12AA</u> <u>G03XC01</u> <u>H05AA02</u> H05BA01 M05BA01 M05BA03 M05BA04 M05BA07 M05BA08 M05BB01 M05BB02 M05BB03 M05BB04 M05BB07 M05BB08 <u>V03AG01</u>
Pancreatic insufficiency	Pancreatic exocrine enzyme replacements	12201	<u>A05AA</u>	A05AA01 A05AA02 <u>A09AA02</u>
Parkinson's disease	Antiparkinsonian agents (dopamine agonists, specified anticholinergics)	221904, 221901, 220101	<u>N04</u>	<u>N01AX03</u> <u>N01BB01</u> N04AA02 N04BA01 N04BA01 N04BB01 N04BC01 N04BC02 N04BC04 N04BC04 N04BC05 N04BC05 N04BC07 N04BD01 N04BX01 N04BX02

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Psychotic illness	Antipsychotics (oral and depot)	222204, 222201, 222208	N05AA01 N05AA02 N05AB02 N05AB02 N05AB06 N05AC01 N05AC02 N05AC04 N05AD01 N05AD01 N05AD08 N05AE04 N05AF01 N05AF04 N05AF05 N05AG01 N05AG02 N05AH01 N05AH02 N05AH03 N05AH04 N05AL01 N05AL05 N05AN01 N05AX08 N05AX12 N05AX13
Pulmonary hypertension, PVD	Endothelin receptor antagonists; Phosphodiesterase Type 5 inhibitors; Prostacyclin analogues; vasodilators	74005, 74007, 74009, 74001	<u>C01DX16</u> <u>C02DB02</u> <u>C02DC01</u> <u>C02KX01</u> <u>C02KX02</u> <u>C04AC02</u> <u>C04AD03</u> <u>C04AX01</u> <u>V03AB22</u>

Reactive airway disease	Inhaled bronchodilators and corticosteroids; anticholinergic agents; mast cell stabilisers; Leukotriene inhibitors; respiratory devices	283001, 283010, 283401, 283410, 281001, 282404, 282402, 284001, 284302, 284502, 285302	<u>R03</u>	<u>C01CA26</u> <u>N06BC01</u> R03AB03 R03AC02 R03AC03 R03AC04 R03AC06 R03AC12 R03AC13 R03AC18 R03BA01 R03BA02 R03BA05 R03BB01 R03BC01 R03BC03 R03CC02 R03CC03 R03CC04 R03CC05 R03CC12 R03DA04 R03DA02 R03DA05
Rheumatoid arthritis	Antirheumatoid agents; TNF inhibitors	190701, 190702	<u>M01C</u>	<u>L04AA13</u> <u>L04AB01</u> M01CB01 M01CB03 M01CB04 M01CC01 <u>M02AB01</u>
Steroids-responsive conditions	Glucocorticoids (systemic corticosteroids)	140701	<u>H02AA</u> <u>H02AB</u>	<u>H01AA01</u> H02AA02 H02AB01 H02AB02 H02AB04 H02AB06 H02AB07 H02AB08 H02AB09 H02AB10

Transplant/ Auto-immune disorders	Immunosuppressants	250701, 250706		<u>L01XE10</u> <u>L04AA06</u> <u>L04AA10</u> <u>L04AD01</u> <u>L04AD02</u> <u>L04AX01</u>
Tuberculosis	Antitubercular agents	161601	<u>J04A</u>	<u>J01MA09</u> J04AA01 J04AB01 J04AB02 J04AB04 J04AB30 J04AC01 J04AD01 J04AD03 J04AK01 J04AK02 J04AM02 <u>J04BA01</u> <u>J04BA02</u>
CVD medication categories:				
Antiplatelet	Antiplatelet agents; coagulation check strips****	40701		<u>B01AB10</u> <u>B01AC04</u> <u>B01AC06</u> <u>B01AC07</u> <u>B01AC22</u> <u>B01AC24</u>
Hyperlipidaemia	Lipid lowering agents	41301, 41304, 41302, 41303, 41308, 73201, 73202, 73203, 73205, 73208	<u>C10AB</u> <u>C10AC</u>	C10AB01 C10AB02 C10AB04 C10AC01 C10AC02 <u>C10AD02</u> <u>C10AD06</u> <u>C10AD52</u> <u>C10AX02</u> <u>C10AX06</u> <u>C10AX09</u>

1			<u>C02A</u>	C02AB01
2				C02AB02
3				C02AC01
4			<u>C02C</u>	C02CA01
5				C02CA04
6				C02CC02
7			<u>C03A</u>	C03AA01
8				C03AA04
9				C03AA07
10				C03AA08
11				C03AB01
12			<u>C03B</u>	C03BA04
13				C03BA08
14				C03BA11
15			<u>C03D</u>	C03DA01
16				C03DB01
17				C03DB01
18				C03DB02
19			<u>C03EA</u>	C03EA13
20		Beta blockers; calcium channel blockers;		<u>C04AB01</u>
21	Ischemic heart	ACE inhibitors; Angiotensin II inhibitors;	70101, 70701, 70702, 70703, 71601,	<u>C04AX02</u>
22	disease/Hypertension	Thiazides; Potassium-sparing agents;	71901, 72201, 72202, 72801, 73107,	
23		combination antihypertensives; diuretics	73104, 73110, 70401, 70705	
24		and other hypertensives (Clonidine,		<u>C07AA01-08</u>
25		Hydralazine)		C07AA01
26				C07AA02
27				C07AA03
28				C07AA05
29				C07AA06
30				C07AA07
31				C07AA12
32			<u>C07AB02-08</u>	C07AB02
33				C07AB03
34				C07AB04
35				C07AB07
36				C07AB08
37			<u>C07AG</u>	C07AG01
38				C07AG02
39			<u>C08CA</u>	C08CA01
40				C08CA02
41				C08CA03
42				C08CA05
43				<u>C08DA01</u>
44				<u>C08DB01</u>
45				<u>C08EX02</u>
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			<u>C09AA</u>	C09AA01
				C09AA02
				C09AA03
				C09AA04
				C09AA06
				C09AA07
				C09AA08
				C09AA10
			<u>C09CA</u>	C09CA01
				C09CA06

* PHARMAC’s modified ATC codes, as available in the core data source and used in classification of indices.

** Suggested mapping to ATC code groups.

***Suggested specific ATC codes based on medications discovered in current NZ Pharmaceutical data for this analysis. Bolded/underlined items are single-code suggestions that do not fall under the groupings in the preceding column.

**** Some or all items coded in the PHARMAC-modified ATC coding system have no corresponding item in the WHO’s ATC coding system.

Supplementary Methods on Multiple Imputation

Sensitivity analysis (text reproduced from body of main paper)

To address the impact of missing covariate data (5.8% of individuals missing ethnicity and/or NZDep quintile), we used multiple imputation to examine whether the associations measured in the main analysis could have been biased due to exclusion of individuals with missing data (complete case analysis). Five imputation datasets were created using chained equations³² (using the mice package in R³³). These datasets imputed missing values for ethnicity and NZDep quintile (as polynomial variables) based on all other variables in the analytical model including exposure variables and outcome variables (multimorbidity status, age group, sex, ethnicity, NZDep quintile, and all outcome variables). The imputation models also included auxiliary information on each person's District Health Board of residence (the 20 administrative divisions of the public health system in NZ, which provides additional information on sub-national distribution of people by ethnicity and socioeconomic deprivation). Further details on this analysis and underlying assumptions are given with Supplementary Table B.

References from main paper:

32. White IR, Royston P, Wood AM. Multiple imputation using chained equations: Issues and guidance for practice. *Stat Med* 2011;30(4):377-99. doi: 10.1002/sim.4067 [published Online First: 2011/01/13]
33. van Buuren S, Groothuis-Oudshoorn K. mice: Multivariate Imputation by Chained Equations in R. *Journal of statistical software* 2011;45(3):1-67.

Supplementary Methods on Assumptions of Multiple Imputation

The following notes assume some familiarity with methods for missing data and multiple imputation: several overview papers have been previously published on this methodology¹⁻³.

In order for multiple imputation of covariates to be valid and useful, a key assumption is that data are missing at random (MAR), which means that the to-be-imputed values can be considered to be missing at random conditional on the variables included in the imputation model.^{1,2} Thus, an imputation process that draws on these conditioning variables (including exposure and outcome variables) to produce imputed values should be able to recover some information to account for the potential profile of those people who are missing some data. It is not possible to determine from a dataset whether data are missing at random or missing not at random (MNAR: i.e. some additional unmeasured information influences whether data are missing).^{2,3} However, including a sufficient number of meaningful variables as predictors in the imputation model process, including exposure and outcome variables, serves to make the missing at random assumption more plausible for a given scenario^{1,3}.

In the current study, we believe on theoretical grounds that the missing data (for ethnicity and socioeconomic status as measured by area of residence using NZDep 2013) are effectively missing at random, conditional on the variables included in our imputation model.

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Firstly, we assume that ethnicity data collected in the routine data sources is more likely to be present for people with multiple health contacts (because these are opportunities to collect ethnicity data in line with NZ's ethnicity data protocols). The imputation models explicitly include information on multimorbidity status and subsequent health outcomes in the imputation process. This means health-status is being used as part of the imputation process, which should lead to valid results for the imputation analysis (in conjunction with other known sources of patterning for ethnicity across NZ, including geographic variation and variation of socioeconomic status by ethnicity).

Secondly, NZDep values (the second missing variable in the regression models) tend to be missing when address information for a given person is either unavailable or incompletely recorded in the Ministry of Health's master databases (and hence geocoding cannot be performed to assign that person with an area-based code), or when there an otherwise-correct address cannot be mapped to the area codes recorded in the measure NZDep. The chances of this second scenario depend upon the discrepancy between the time at which a person's address is measured (usually the most recent update to their health record) and the timing of the specific five-yearly census from which the NZDep measure was derived (in this case, the 2013 census conducted in March 2013).

Supplementary Table B below includes both the complete-cases results of the regression models (top half, reproducing results from Table 4 of the main paper) and also the results of the analysis of the multiply-imputed datasets (bottom half of Sup. Table B) following the analytical procedures given in the main paper (as reproduced above). As can be seen, and as reported in the main paper, the results are almost identical in the two analyses: point estimates are marginally higher in the imputed-data results, but not substantively different.

References for Supplementary Methods text:

1. Donders AR, van der Heijden GJ, Stijnen T, et al. Review: a gentle introduction to imputation of missing values. *J Clin Epidemiol* 2006;59(10):1087-91. doi: 10.1016/j.jclinepi.2006.01.014 [published Online First: 2006/09/19]
2. Sterne JA, White IR, Carlin JB, et al. Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. *BMJ* 2009;338:b2393. doi: 10.1136/bmj.b2393 [published Online First: 2009/07/01]
3. Harel O, Zhou XH. Multiple imputation: review of theory, implementation and software. *Stat Med* 2007;26(16):3057-77. doi: 10.1002/sim.2787

Supplementary Table B. Results from original complete-case analysis (top panel, Table 4 from main paper) and from analysis of multiply imputed data (n=5 imputation datasets).

Model†	Odds ratio (95% CI) for risk of outcome with multimorbidity*					
	Hospital discharge definition			Pharmaceutical dispensing definition		
	Mortality	ASH‡	Admission§	Mortality	ASH‡	Admission§
COMPLETE CASE ANALYSIS						
Unadjusted model	17.6 (17.2, 18.1)	8.4 (8.3, 8.5)	5.6 (5.6, 5.7)	14.7 (14.2, 15.2)	5.5 (5.5, 5.6)	3.7 (3.7, 3.7)
Adjusted age, sex	4.8 (4.7, 5.0)	4.9 (4.9, 5.0)	3.6 (3.5, 3.6)	4.0 (3.9, 4.2)	3.6 (3.6, 3.7)	2.6 (2.6, 2.7)
+ adjust ethnicity	4.7 (4.6, 4.8)	4.7 (4.6, 4.7)	3.5 (3.5, 3.5)	3.9 (3.8, 4.1)	3.6 (3.5, 3.6)	2.6 (2.6, 2.6)
+ adjust NZDep quintile	4.6 (4.5, 4.7)	4.6 (4.5, 4.6)	3.5 (3.4, 3.5)	3.9 (3.7, 4.0)	3.5 (3.5, 3.6)	2.6 (2.6, 2.6)
MULTIPLE IMPUTATION ANALYSIS						
Unadjusted model	18.0 (17.5, 18.4)	8.7 (8.6, 8.9)	5.8 (5.8, 5.9)	14.8 (14.3, 15.3)	5.7 (5.6, 5.8)	3.8 (3.8, 3.8)
Adjusted age, sex	4.9 (4.8, 5.0)	5.1 (5.1, 5.2)	3.7 (3.7, 3.7)	4.1 (4.0, 4.2)	3.7 (3.7, 3.8)	2.7 (2.7, 2.7)
+ adjust ethnicity	4.8 (4.6, 4.9)	4.8 (4.8, 4.9)	3.6 (3.6, 3.7)	4.0 (3.9, 4.1)	3.7 (3.6, 3.7)	2.7 (2.7, 2.7)
+ adjust NZDep quintile	4.7 (4.6, 4.8)	4.7 (4.7, 4.8)	3.6 (3.6, 3.6)	3.9 (3.8, 4.1)	3.6 (3.6, 3.7)	2.7 (2.6, 2.7)

* Reference group is individuals without multimorbidity (i.e. either zero or only one long-term conditions identified)

† All models run on complete-case data only (n=3,288,646; total of n=201,101 missing ethnicity &/or NZDep)

‡ Ambulatory sensitive hospitalisation (ASH)

§ Non-maternity admissions with at least an overnight stay.

Note: Complete-cases analysis reproduces results shown in Table 4 of main paper (regression results for people with complete data for all covariates included in the fully-adjusted model). 5.8% of individuals were missing ethnicity and/or NZDep quintile data in the complete-case analysis.

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page # / note
Title and abstract	1	(a) Indicate the study’s design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4-5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(a) Cohort study—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5
		Case-control study—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls	
		Cross-sectional study—Give the eligibility criteria, and the sources and methods of selection of participants	
		(b) Cohort study—For matched studies, give matching criteria and number of exposed and unexposed	
Case-control study—For matched studies, give matching criteria and the number of controls per case			
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5
Bias	9	Describe any efforts to address potential sources of bias	(discussion)
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	6-7
		(b) Describe any methods used to examine subgroups and interactions	n/a
		(c) Explain how missing data were addressed	p.6
		(d) Cohort study—If applicable, explain how loss to follow-up was addressed	n/a
		Case-control study—If applicable, explain how matching of cases and controls was addressed	
		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	p. 7 (imputation)

Results

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	n/a (cross-sectional)
		(c) Consider use of a flow diagram	Not included (one-step selection)
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	
		(b) Indicate number of participants with missing data for each variable of interest	Table 1, Table 4 (footnotes to each)
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	P6. For prospective element
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	p. 8, Table 3
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	n/a
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	n/a
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	p. 7-11, all tables and figures.
		(b) Report category boundaries when continuous variables were categorized	Table 1, Figs 1-4
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Absolute risk on p. 7-11, Table 4
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	p. 11, Supp. Table B

Discussion

Key results	18	Summarise key results with reference to study objectives	p. 14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	p. 14-15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	p. 14-16
Generalisability	21	Discuss the generalisability (external validity) of the study results	p. 16

Other information

Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	p3 and online statement
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*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Epidemiology of multimorbidity in New Zealand: A cross-sectional study using national-level hospital and pharmaceutical data

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-021689.R2
Article Type:	Research
Date Submitted by the Author:	10-Apr-2018
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TITLE: Epidemiology of multimorbidity in New Zealand: A cross-sectional study using national-level hospital and pharmaceutical data

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ABSTRACT

OBJECTIVES: To describe the prevalence of multimorbidity (presence of two or more long-term health conditions) in the New Zealand (NZ) population, and compare risk of health outcomes by multimorbidity status.

DESIGN: Cross-sectional analysis for prevalence of multimorbidity, with one-year prospective follow-up for health outcomes.

SETTING: NZ general population using national-level routine health data on hospital discharges and pharmaceutical dispensing.

PARTICIPANTS: All NZ adults (aged 18+, n=3,489,747) with an active National Health Index (NHI) number at the index date (1st Jan 2014).

OUTCOME MEASURES: Prevalence of multimorbidity was calculated using two data sources: prior routine hospital discharge data (61 ICD-10 coded diagnoses from the M3 multimorbidity index); and recent pharmaceutical dispensing records (30 conditions from the P3 multimorbidity index).

METHODS: Prevalence of multimorbidity was calculated separately for the two data sources, stratified by age group, sex, ethnicity, and socioeconomic deprivation, and age-/sex-standardised to the total population. One-year risk of poor health outcomes (mortality, ambulatory sensitive hospitalisation (ASH), and overnight hospital admission) was compared by multimorbidity status using logistic regression adjusted for confounders.

RESULTS: Prevalence of multimorbidity was 7.9% using past hospital discharge data, and 27.9% using past pharmaceutical dispensing data. Prevalence increased with age, with a clear socioeconomic gradient and differences in prevalence by ethnicity. Age/sex standardised one-year mortality risk was 2.7% for those with multimorbidity (defined on hospital discharge data), and 0.5% for those without multimorbidity (age/sex adjusted OR = 4.8, 95% CI 4.7, 5.0). Risk of ASH was also increased for those with multimorbidity (e.g. pharmaceutical discharge definition: age/sex-standardised risk 6.2%, compared to 1.8% for those without multimorbidity; age/sex-adjusted OR = 3.6, 95% CI 3.5, 3.6).

CONCLUSIONS: Multimorbidity is common in the NZ adult population, with disparities in who is affected. Providing for the needs of individuals with multimorbidity requires collaborative and coordinated work across the health sector.

KEYWORDS: multimorbidity, long-term conditions, chronic conditions, epidemiology

Strengths and limitations of the study

- This study uses national-level data for nearly 3.5 million New Zealand adults to provide robust estimates of the prevalence of multimorbidity.
- Multimorbidity was defined using existing methods to classify and code long-term health conditions, based on well-established data sources for prior hospital discharge and pharmaceutical dispensing.
- Health outcome measures (mortality and hospital admission) were available for everyone in the study population.
- Due to the nature of the data sources, not all long-term health conditions could be measured: the estimates include only conditions recorded during a past hospital admission or those long-term conditions which can be treated by medication (and where medications are specific to treating a condition).
- Results may be only partially comparable with those studies from other countries that have used a primary-care based sampling frame or data source to estimate prevalence of multimorbidity.

INTRODUCTION

Health care delivery in secondary-care settings has typically been dominated by systems that focus on the treatment or management of a single disease,¹ such as cancer or diabetes, with less attention paid to other health conditions (which are typically conceptualised as comorbidities). Recently, more attention has been given towards the concept of multimorbidity, defined as the co-presence of two or more long-term health conditions,^{2,3} as a framework for viewing a patient's health needs from a more holistic management perspective.⁴⁻⁶ While such management is considered best practice in primary care settings, the quality of care provided in both secondary and primary care settings could be improved by encouraging a greater emphasis on this approach and considering the complex needs of patients with multimorbidity.⁷⁻⁹

This view of multimorbidity also requires consideration of the social and economic determinants of health that lie upstream of poor health generally.^{10,11} Long-term conditions are patterned by these determinants of health such as greater exposure to social, environmental or workplace risk factors, which in turn often pattern individual-level risk factors e.g. smoking, poor diet, lack of exercise, and poorer access to healthcare resources in the socioeconomically disadvantaged.

At an individual level, those with multimorbidity have poorer health outcomes, including increased risk stemming from polypharmacy, worse functional status, and lower quality of life.^{2,12,13} The implications of multimorbidity for health systems have been well described: expenditure on health care in high-income countries is dominated by the needs of those with multiple long-term conditions.^{5,14} Furthermore, while multimorbidity is not restricted to the elderly, it is more prevalent amongst older people.^{2,3} Therefore the healthcare demands and costs associated with multimorbidity will continue to rise as populations age,¹⁵ though the rising prevalence of multimorbidity does not appear to be solely driven by aging populations.¹⁶

There have been many prevalence studies of multimorbidity, as described in several systematic reviews.^{2,3,12,13} Studies have generally focussed on multimorbidity in specific populations (e.g. the elderly^{17,18}, or amongst hospitalised patients¹⁸); or examined the general population, either amongst registered populations using existing patient databases^{19,20} or using surveys of the general population;¹⁵ or have measured multimorbidity during primary care interactions.²¹

A 2012 systematic review³ looked at variations in the prevalence of multimorbidity by country and research setting (e.g. primary health care patients, or across the general population.) Unsurprisingly, studies that sampled individual patients during primary care consultations have typically reported higher prevalence of multimorbidity compared to studies that used broader health-system based populations as the denominator (e.g. registered patients).³

This review made two major recommendations for studying multimorbidity: firstly, use a broad sample frame that matches the appropriate target population; and secondly, consider a reasonably comprehensive list of long-term conditions to capture the sheer variety of specific health needs that arise in long-term conditions (with a lower bound of 12 eligible conditions suggested as a minimum).³

Our primary objective was to describe the prevalence of multimorbidity for the general adult population in New Zealand (NZ), defining multimorbidity status using past hospital discharge and

pharmaceutical dispensing records. To examine health inequities, we also analysed the patterning of multimorbidity by major sociodemographic and socioeconomic groupings. As a secondary objective, we examined subsequent health outcomes for those with multimorbidity, including mortality, ambulatory sensitive hospitalisations (ASH) and overnight admissions to hospital.

METHODS

Study design, setting and participants

This study is a cross-sectional prevalence study of multimorbidity across the NZ adult population, defined at 1st January 2014, using routinely collected, national level administrative health data. We also examined subsequent health outcomes for the year following this index date. Study size was determined by the total identified population at this index date.

The target study population was all NZ adults (aged 18+), operationally defined as individuals with an active National Health Index (NHI) number, based on active enrolment with a Primary Health Organisation (PHO) or recent interaction with the NZ health system in the year prior to the index date (n=3,489,747). No additional inclusion or exclusion criteria were applied. Further details are given under data sources below. This target population covers the vast majority of New Zealanders (it is estimated that around 94% of the entire population are enrolled with a PHO²², and so the actual coverage should be in excess of 94% when including additional individuals who meet the recent-interaction criteria for an active NHI number).

Patient and Public Involvement

Patients and members of the public were not involved in the design or conduct of this study.

Data sources

All data were sourced from the national collections as maintained by the NZ Ministry of Health.²² The population denominator and sociodemographic information were derived from the master NHI table. This source includes information on date of birth, sex, ethnicity, and place of residence, and can be linked to other national health data using the unique NHI identifier.

Information on long-term conditions was sourced for an extended period prior to the index date from (1) the National Minimum Data Set (NMDS), which captures all publicly funded hospital discharges in NZ (and some privately funded), with diagnostic information relevant to the admission coded using ICD-10 codes; and (2) the Pharmaceutical collection, which includes all community-dispensed prescriptions across NZ, with medications coded using a modified version of the ATC classification system.^{23 24} The past hospital discharge data thus provides a measure for the general population of long-term conditions that have been recorded during hospital admissions (over an extended period of five years to capture all relevant long-term conditions); while the pharmaceutical data provides a similar measure for the general population (using a one-year lookback period, assuming that these long-term conditions are under active management). Both data sources use the total adult denominator when calculating rates for the same population.

Long-term conditions were identified using the condition lists developed for the M3 index (for prior hospital discharge data,²⁵ based on all diagnoses recorded for discharges in the five-year lookback

period) and the P3 index (for community pharmaceutical data (see Supplementary Table A), based on dispensings in a one year lookback period from the index date). Both indices were developed for considering mortality risk in population health analyses, with the individual conditions chosen based on chronicity, expected impact on mortality, and other long term impacts on health. The M3 index includes a total of 61 conditions, with the list of conditions intended to capture long-term conditions known to have some impact on mortality and/or morbidity. The P3 index includes a different, shorter list of 30 conditions, as the underlying pharmaceutical dispensing data can only capture conditions for which pharmaceutical treatment is possible. Furthermore, since some medications are used to treat multiple disparate conditions, it is not always possible to determine the precise condition or indication for a given medication. These medications with multiple common indications were thus excluded in the creation of the P3 index. Both of these indices are described in full detail elsewhere for the M3 index²⁵ and in Supplementary Table A for the P3 index, including full details of the exact codes included in their definitions for any condition.

Information on deaths during the follow-up period was drawn from the NZ Mortality Collection.

Variables

Multimorbidity was defined as having at least two conditions from the M3 or P3 condition list. Results are reported separately based on these two different data sources, as the conditions coded by each index do not fully align with each other. In addition to prevalence of multimorbidity, the numbers of identified conditions are reported using medians and interquartile range.

Prevalence estimates are reported stratified by several sociodemographic and socioeconomic factors. Age at the index date and sex were defined using information from the NHI master table (age grouped as 18-24, 25-34, 35-44, 45-54, 55-64, 65-74, 75-84, and 85+). Prevalence by broad ethnic groups (Māori, Pacific, Asian, European and Middle-Eastern/Latin American/African/Other [MELAA/Other]) is presented using a modified total ethnicity approach based on self-identified health as recorded in the NHI master table, in line with best practice in NZ health settings.²⁶ Total ethnicity reporting means that individuals who self-identify with more than one ethnic group were counted in both numerator and denominator for each of those groups: to allow some comparison in prevalence estimates, the European group was treated as a mutually exclusive group (i.e. containing individuals who only self-identified as NZ European or European). For regression analysis, ethnicity was prioritised so that individuals were only assigned to one group (in the order noted above) following standard practice.²⁶

Socioeconomic status was measured using the NZDep 2013 index,²⁷ an area based measure of socioeconomic deprivation produced from relevant information in the NZ census. This was matched to individual's health records based on their geocoded residential address in the NHI master record: in some cases this information was missing and hence an NZDep score could not be assigned to a person's record (missing data reported in Table 1).

We also considered several potential adverse outcomes from multimorbidity during the one-year follow-up period (1st January 2014 to 31 December 2014). Data was available for all participants across this period. All-cause mortality was considered alongside ambulatory sensitive hospitalisation (ASH admissions) and overnight hospital admissions. ASH admissions were defined based on a primary diagnosis in a specified list^{28 29} where the admission type was defined as either acute or

arranged (i.e. excluding elective admissions, except in the case of dental procedures which are always coded as ASH regardless of admission type). Overnight hospital admissions were any admissions that included an overnight stay in hospital, with the exclusion of maternity related events (defined as any admission with a primary diagnosis ICD code starting with “O”).

Statistical methods

Data coding and preparation was conducted in SAS 9.4 (SAS Institute, Cary, NC); all subsequent analyses were conducted using R 3.2 (R Foundation, Vienna, Austria).

Prevalence estimates for the NZ adult population are reported at the index date as crude percentages. For reporting of prevalence of multimorbidity stratified by other sociodemographic factors, we directly age- and sex-standardised estimates for each sub-group to reflect the total adult NZ age/sex distribution (as calculated for the entire study population) using R’s epitools package.³⁰ Prevalence for the total NZ adult population is also reported following direct age-standardisation to the World Health Organisation (WHO) world standard.³¹

We also compared adverse outcomes (death, ambulatory sensitive hospitalisation [ASH], and overnight hospitalisation) within one year between individuals with and without multimorbidity, again in separate analyses with multimorbidity defined based on hospital diagnosis data or pharmaceutical dispensing data. Risks of outcomes within one year of the index date are initially presented as crude and age/sex-standardised risks for each outcome. We also report odds ratios (from binary logistic regression) comparing the odds of each outcome in models where we sequentially adjusted for confounder variables. The first model for each outcome presents unadjusted odds ratios; the second model adjusts for age group and sex; the third model additionally adjusts for prioritised ethnicity; and the fully-adjusted fourth model adds in adjustment for socioeconomic status using NZDep2013 (in quintiles as a categorical variable). Regression analysis was restricted to individuals with complete information on all covariates (complete case analysis).

Sensitivity analysis

To address the impact of missing covariate data (5.8% of individuals missing ethnicity and/or NZDep quintile), we used multiple imputation to examine whether the associations measured in the main analysis could have been biased due to exclusion of individuals with missing data (complete case analysis). Five imputation datasets were created using chained equations³² (using the mice package³³ in R). These datasets imputed missing values for ethnicity and NZDep quintile (as polynomial variables) based on all other variables in the analytical model including exposure variables and outcome variables (multimorbidity status, age group, sex, ethnicity, NZDep quintile, and all outcome variables). The imputation models also included auxiliary information on each person’s District Health Board of residence (the 20 administrative divisions of the public health system in NZ, which provides additional information on sub-national distribution of people by ethnicity and socioeconomic deprivation). Further details on this analysis and underlying assumptions are given with Supplementary Table B.

RESULTS

Table 1 gives the sociodemographic profile of the 3.49 million NZ adults in the study population at the index date (1st January 2014). Table 2 gives a list of the top 15 condition categories (as single conditions) identified across the population (i.e. not just amongst those with multimorbidity) for both the hospital diagnosis data (based on the M3 index categories) and the pharmaceutical dispensing data (based on the P3 index categories).

Prevalence estimates for multimorbidity in the adult population at the index date are also presented in Table 1, for definitions of multimorbidity drawing from each of the two data sources (past hospitalisation discharge records and past pharmaceutical dispensing). Across the entire identified NZ adult population, 7.9% of the population were defined as having multimorbidity when using the past-five-years hospital diagnosis data source; prevalence was considerably higher at 27.9% when using the past-year pharmaceutical dispensing data source. When age-standardised to the WHO standard age structure, these prevalences were 6% and 23% respectively.

As expected, the prevalence of multimorbidity increased with age for both definitions, as also shown in Figure 1. Prevalence of multimorbidity was consistently higher based on pharmaceutical dispensing data compared to hospital admission data, with the difference widening in the older age groups. Multimorbidity based on hospital data was higher for males than females (8.6% and 7.4%, age standardised); while females had higher prevalence based on pharmaceutical dispensing (30.7% compared to 24.8% for males, age-standardised). Differences between males and females in patterns of multimorbidity by age are shown in Figure 2: the higher prevalence using hospital discharge data amongst males becomes manifest by the 55-64 age group, while higher prevalence for females compared to males based on pharmaceutical dispensing data was apparent across all age groups.

The crude prevalence of multimorbidity based on hospital data (Table 1, middle set of columns) was roughly similar across NZ European, Māori and Pacific populations (8.6 to 9.3%) and lower for Asian and MELAA/Other groups (4.6% and 4.7%). This was partially due to the NZ European group having an older population distribution: following age- and sex-standardisation, prevalence of multimorbidity was higher for Māori and Pacific ethnic groups (13.4% and 13.8% prevalence respectively) than for NZ European (7.6% prevalence), and the Asian and MELAA/Other groups (6.9 and 8.7% respectively) were also more in line with the NZ European prevalence. Figure 3 gives age-stratified estimates of multimorbidity by total ethnicity group, which shows early divergence by ethnicity in younger age groups but relatively similar trajectories of prevalence as age increases.

Table 1. Sociodemographic and socioeconomic description of study population at index date (1st Jan 2014)

Variable	Group	Total* n (column %)	Prevalence of Multimorbidity			
			Hospital Discharge data (last five years)		Pharmaceutical data (last year)	
			n (%)	Standardised† %	n (%)	Standardised† %
Total	Total	3,489,747 (100.0)	275,706 (7.9)	7.9	972,222 (27.9)	27.9
Age group	18-24	454,511 (13.0)	7,258 (1.6)	1.6	36,625 (8.1)	8.1
	25-34	605,263 (17.3)	12,334 (2.0)	2.0	69,041 (11.4)	11.4
	35-44	621,645 (17.8)	18,978 (3.1)	3.1	104,296 (16.8)	16.7
	45-54	646,669 (18.5)	33,987 (5.3)	5.3	160,862 (24.9)	24.9
	55-64	525,600 (15.1)	48,702 (9.3)	9.2	199,362 (37.9)	38.0
	65-74	366,866 (10.5)	62,869 (17.1)	17.1	201,807 (55.0)	55.0
	75-84	193,497 (5.5)	59,116 (30.6)	30.7	139,099 (71.9)	71.7
	85+	75,696 (2.2)	32,462 (42.9)	43.3	61,130 (80.8)	80.4
Sex	Female	1,807,908 (51.8)	135,615 (7.5)	7.3	561,921 (31.1)	30.7
	Male	1,681,839 (48.2)	140,091 (8.3)	8.6	410,301 (24.4)	24.8
Total Ethnicity‡	NZ European	2,292,963 (69.6)	197,471 (8.6)	7.6	725,030 (31.6)	29.0
	Māori	402,188 (12.2)	37,111 (9.2)	13.4	97,337 (24.2)	31.7
	Pacific	226,503 (6.9)	21,108 (9.3)	13.8	49,645 (21.9)	29.8
	Asian	360,349 (10.9)	16,726 (4.6)	6.9	68,926 (19.1)	24.3
	MELAA/Other	44,056 (1.3)	2,091 (4.7)	8.7	9,087 (20.6)	29.9
NZDep Quintile§	1	669,348 (19.2)	37,217 (5.6)	5.8	167,609 (25.0)	25.1
	2	653,071 (18.8)	44,000 (6.7)	6.7	173,294 (26.5)	26.3
	3	672,889 (19.3)	52,417 (7.8)	7.3	191,645 (28.5)	27.5
	4	737,521 (21.2)	66,749 (9.1)	8.7	222,336 (30.1)	29.6
	5	748,339 (21.5)	74,548 (10.0)	10.8	215,689 (28.8)	30.9

* Total column reports number of people in each sociodemographic category and their proportion of the total adult population at the index date.

† Standardised to age and sex profile of total study population (aged 18+; age groups as presented). All standardised confidence intervals were narrower than +/- 0.2%.

‡ People identifying with multiple ethnic groups are counted in each of these groups (and so total can sum to > 100%). n=192,910 individuals had no ethnicity recorded.

§ A total of 140,056 individuals had no NZDep quintile available (could not be matched to a valid NZDep area)

Table 2. Prevalence of top 15 individual condition categories (study group total N = 3,489,747) based on hospital admission data (top panel) and pharmaceutical dispensing data (bottom panel).

Condition (hospital discharge data, last five years,)	n	Prevalence (%)
Cardiac arrhythmia	76,469	2.2
Diabetes complicated	75,957	2.2
Hypertension uncomplicated	62,030	1.8
Metabolic disorder	57,937	1.7
Bowel disease inflammatory	56,335	1.6
Cardiac disease (other)	54,508	1.6
Chronic pulmonary disease	48,417	1.4
Coagulopathy and other blood disorders	43,329	1.2
Cerebrovascular disease	40,619	1.2
Myocardial infarction	36,811	1.1
Eye problem long term	36,266	1.0
Congestive heart failure	33,329	1.0
Angina	33,147	0.9
Major psychiatric disorder	32,687	0.9
Intestinal disorder	32,457	0.9

Condition (pharmaceutical dispensing data, last year)	n	Prevalence (%)
Gastric acid disorder	514,562	14.7
CVD (Low Risk*)	495,386	14.2
Depression	418,512	12
Reactive airway disease	383,652	11
Anxiety and tension	318,563	9.1
CVD (Moderate Risk†)	302,317	8.7
Steroids responsive conditions	279,394	8.0
Diabetes	186,186	5.3
Hypothyroidism	113,098	3.2
Congestive heart failure	94,342	2.7
Anaemias	89,336	2.6
Psychotic illness	81,788	2.3
Epilepsy	77,040	2.2
Ischaemic heart disease/Angina	72,942	2.1
Anticoagulation	70,753	2.0

* Medication from one cardiovascular disease category

† Medication from two cardiovascular disease categories

Crude ethnic group differences in prevalence based on pharmaceutical dispensing (Table 1, right hand set of columns) were also confounded by age. Crude prevalence appeared relatively high in NZ European (31.6%) compared to the other ethnic groups (19.1-24.2%), but following age standardisation these differences were less pronounced (prevalence between 29 and 32% for all groups except Asian, with a standardised prevalence of 24.3%). Age-stratified ethnic patterns of multimorbidity based on pharmaceutical dispensing data are shown in Figure 3.

Multimorbidity was also more common amongst those in higher socioeconomic deprivation areas (based on NZDep2013), with standardised prevalence based on hospital diagnoses rising from 5.8% (least deprived quintile) to 10.8% (most deprived quintile); and for pharmaceutical based definitions from 25.1% (least deprived) to 30.9% (most deprived). These patterns were consistent across the age spectrum (Figure 4.)

Those with multimorbidity were at substantially higher risk of an adverse outcome in the year following the index date (mortality, ASH admission, non-maternity overnight admission). Table 3 gives the crude and age-/sex-standardised risk of each adverse outcome by multimorbidity status. Absolute risk was consistently higher across all outcomes for the multimorbidity group based on the past hospital diagnosis definition than for the past pharmaceutical dispensing definition. Figure 5 plots the age-/sex-standardised risks for each outcome according to multimorbidity status, based on the two data sources.

Table 4 shows the odds ratios for each adverse outcome by multimorbidity status, from logistic regression models. Unadjusted estimates (first row of Table 4) were largely confounded by age and sex: further adjustment for ethnicity and socioeconomic deprivation (NZDep) had minimal impact on estimates of comparisons by multimorbidity status. All results in the following text are from the complete-case analysis for the fully adjusted model (bottom row of Table 4).

All three outcomes were substantially more common for those with multimorbidity than those without. While one-year mortality was just under 1% for the total adult population, those with multimorbidity had around a 3 to 5-fold higher risk of death (fully adjusted OR = 3.9, 95% CI 3.7, 4.0 for the pharmaceutical dispensing definition; and 4.6, 95% CI 4.5, 4.7 for the hospital diagnosis definition.) Fully adjusted odds ratios for the ASH and non-maternity hospital admission outcomes also indicated higher risk of hospitalisation for those with multimorbidity: odds ratios from models using the hospital diagnosis definition were again higher than the corresponding OR from the models using the pharmaceutical dispensing definition (Table 4).

The analyses looking at health outcomes were repeated following multiple imputation for missing data on ethnicity and socioeconomic deprivation (5.8% of cases). As shown in Supplementary Table B, adjusted estimates following imputation were not substantially different from the estimates from complete-case analysis. For example, for the analysis of mortality risk according to multimorbidity defined on hospital-discharge data: complete case analysis OR = 4.6 (95% CI 4.5, 4.7); multiple-imputation pooled OR = 4.7 (95% CI 4.6, 4.8). Other estimates from the imputed data analysis were also of similar magnitude to the main results in Table 4 (Supplementary Table B).

Table 3. Crude and age/sex standardised risk of adverse outcomes within 12 months of index date.

Outcome	Total population (N=3,489,747)	Risk of outcome in following year			
		Hospital discharge data definition		Pharmaceutical dispensing data definition	
		Multimorbid (N=275,706)	Not multimorbid (N=3,214,041)	Multimorbid (N=972,222)	Not multimorbid (N=2,517,525)
		n (crude %) [standardised %]*	n (crude %) [standardised %]*	n (crude %) [standardised %]*	n (crude %) [standardised %]*
Mortality	29,642 (0.8%)	17,536 (6.4%) [2.7%]	12,106 (0.4%) [0.5%]	25,131 (2.6%) [1.3%]	4,511 (0.2%) [0.4%]
ASH admission†	116,522 (3.3%)	45,509 (16.5%) [13.2%]	71,013 (2.2%) [2.4%]	78,347 (8.1%) [6.2%]	38,175 (1.5%) [1.8%]
Overnight admission‡	327,825 (9.4%)	88,285 (32.0%) [27.5%]	239,540 (7.5%) [7.9%]	183,406 (18.9%) [15.7%]	144,419 (5.7%) [6.5%]

Note. Confidence intervals are not printed: for crude risk, the margin of error on the 95% CI was $\leq 0.1\%$; for adjusted risk, $\leq 0.3\%$.

* Age- and sex-standardised to total study population profile.

† Ambulatory sensitive hospitalisation (ASH)

‡ Non-maternity admissions with at least an overnight stay.

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Table 4. Odds ratios for increased risk of mortality/hospital admission with multimorbidity (by multimorbidity defined using past hospital discharge or pharmaceutical dispensing data) from unadjusted and adjusted logistic regression models.

Model†	Odds ratio (95% CI) for risk of outcome with multimorbidity*					
	Hospital discharge definition			Pharmaceutical dispensing definition		
	Mortality	ASH‡	Admission§	Mortality	ASH‡	Admission§
Unadjusted model	17.6 (17.2, 18.1)	8.4 (8.3, 8.5)	5.6 (5.6, 5.7)	14.7 (14.2, 15.2)	5.5 (5.5, 5.6)	3.7 (3.7, 3.7)
Adjusted age, sex	4.8 (4.7, 5.0)	4.9 (4.9, 5.0)	3.6 (3.5, 3.6)	4.0 (3.9, 4.2)	3.6 (3.6, 3.7)	2.6 (2.6, 2.7)
+ adjust ethnicity	4.7 (4.6, 4.8)	4.7 (4.6, 4.7)	3.5 (3.5, 3.5)	3.9 (3.8, 4.1)	3.6 (3.5, 3.6)	2.6 (2.6, 2.6)
+ adjust NZDep quintile	4.6 (4.5, 4.7)	4.6 (4.5, 4.6)	3.5 (3.4, 3.5)	3.9 (3.7, 4.0)	3.5 (3.5, 3.6)	2.6 (2.6, 2.6)

* Reference group is individuals without multimorbidity (i.e. either zero or only one long-term conditions identified)

† All models run on complete-case data only (n=3,288,646; total of n=201,101 missing ethnicity &/or NZDep)

‡ Ambulatory sensitive hospitalisation (ASH)

§ Non-maternity admissions with at least an overnight stay.

DISCUSSION

These results present the first nation-wide report of the prevalence of multimorbidity in nearly 3.5 million New Zealand adults. Over one-quarter of the adult population of NZ had multimorbidity when defined from pharmaceutical dispensing data in the last year (27.9%), although estimates were consistently lower when based on past hospital discharge data over the previous five years (prevalence of 7.9% of all adults). Multimorbidity was more common amongst older people, those living in areas of higher socioeconomic deprivation, and in Māori and Pacific ethnic groups. People with multimorbidity were at higher risk of subsequent adverse outcomes (death and ASH or overnight hospitalisation) in the one-year follow-up period, even following adjustment for confounding from age and other sociodemographic factors.

The prevalence estimates for multimorbidity were generally consistent with international results: the pharmaceutical dispensing based estimate (27.9%) was firmly within estimates of prevalence from those studies that looked at a relatively broad range of age groups from early adulthood – these have typically ranged from 14-40%, with most studies reporting a prevalence between 20% and 30%.²³ Estimates from low and middle income countries have tended to be lower, supporting the hypothesis of epidemiological transition as an important driver in the prevalence of long-term disease,³⁴ though methodological variations may explain this difference. These results are concordant with recent studies in countries with similar population structures. Recent estimates from the United States put multimorbidity in the general population at around 22 to 26%, based on record linkage and survey data respectively.^{20 35} In Canada, survey estimates from the general population have recently been put as high as 59%³⁶ or as low as 13%.³⁷ For future comparisons, the prevalence estimates following age standardisation to the WHO age standard were 6% and 23% respectively for definitions based on the hospital discharge and pharmaceutical dispensing data sources.

In Australia, the most recent national population estimates demonstrate a multimorbidity prevalence of around 33%³⁸ using primary-care attendance numerators and population denominators. A regional Australian study from New South Wales of adults aged 45 and over found prevalence of 36.1 to 37.4%, based on pharmaceutical claims data and survey data respectively; and a prevalence of 19.3% based on past hospital discharge data.¹⁹ Restricting our own data to ages 45 and above returned a prevalence of 42.2% based on pharmaceutical dispensing data, and 13.1% based on hospital discharge data (not shown).

One result of interest for the regression analyses was that there was little change in the magnitude of the associations (between multimorbidity and each health outcome) when adjusting for ethnicity and socioeconomic deprivation (on top of adjustment for age group and sex). This is suggestive that ethnicity and socioeconomic deprivation were not substantial confounders of the association between multimorbidity and subsequent outcomes: it is important to note that the results of the fully-adjusted regression models (not presented) indicated that these two factors were independently associated with the outcome, such that there was still evidence for ethnic inequities and a socioeconomic gradient in outcomes.

The key strengths of this analysis include the wide coverage of the NZ population, covering the vast majority of NZ adults engaged with the health system. The classification and coding of conditions in both the hospital discharge and pharmaceutical dispensing datasets also followed well-delineated methods²⁵ that are reproducible across time and different countries. These two data sources provide complementary definitions of what it means to have multimorbidity.

The key weaknesses are discussed below with respect to the utility of these two data sources. It is worth noting that neither the hospital nor pharmaceutical data source perfectly align with the prevalence of multimorbidity that could be determined from primary care interaction data; however, the national coverage and internal consistency of the hospitalisation and dispensing data sources used in this study improve the generalisability and utility of these data sources above what could be discovered from more locally-held primary care data sources, and the pharmaceutical

1 dispensing data should provide a reasonable approximation for the prevalence of multimorbidity from primary care
2 data. Unfortunately in NZ there is no national collation of primary care data from which the prevalence of
3 multimorbidity can be calculated, and so primary-care level definitions of multimorbidity are not feasible at a
4 national level.

5
6 A second issue arising from the data sources was missing data for the regression models (which was 5.8% of total
7 group missing ethnicity and/or deprivation measure). While there is no uniform consensus on when the amount of
8 missing cases in a regression analysis is likely to bias results, in methodological work the threshold for considering
9 the impact of missing data typically starts at around 10% of cases having missing data (e.g. ^{39 40}). Furthermore,
10 regression models for complete cases (i.e. those with all covariate data available) that adjust for covariates
11 potentially related to missingness (including exposure and confounder variables) have been demonstrated to be
12 unbiased in comparison to more complex analytical methods (e.g. ⁴¹). Our sensitivity analysis using multiple
13 imputation suggested that the adjusted complete-case logistic regression results presented in Table 4 were not
14 biased compared to using multiple imputation.
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17 The final issue is that the data sources used cover adults defined as being engaged with the NZ health system (either
18 through enrolment with a PHO, estimated to cover around 94% of the population; or having used publicly funded
19 health services in the year prior to the index date). It is only possible to speculate about those individuals who are
20 not covered in these data sources: however, we do know that they will not have been in contact with health services
21 in the period used to define multimorbidity, and hence would not be able to meet the operational definitions of
22 multimorbidity used in this study (as these are based on hospital admissions and pharmaceutical dispensing).
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25 The difference in prevalence estimates when using hospital admission and pharmaceutical dispensing data sources
26 has implications for future research and planning. Using past hospital admission data identifies a smaller group of
27 individuals with multimorbidity, but this group is at particularly elevated risk of subsequent poor outcomes
28 (following adjustment for confounders like age and sex). This is highly suggestive of a more severe level of
29 multimorbidity, which may be additionally captured in other analyses by accounting for recent hospital admission as
30 a separate risk factor variable. The appropriate choice of data source for considering multimorbidity based on
31 routine data will ultimately depend on both data availability and the study question being addressed. The two
32 systems also differ regarding the most commonly captured conditions: as one key example, mental health conditions
33 were considerably more prominent when using the pharmaceutical definition than the hospitalisation definitions.
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37 The number of long-term conditions used in defining multimorbidity is known to impact on the measured
38 prevalence: a systematic review recommended a minimum of 12 conditions to facilitate comparable estimates
39 across studies. ³ The conditions included in the current study were selected as reflecting long-term conditions with
40 some impact on subsequent serious health outcomes²⁵, and as such the definition of multimorbidity used here
41 strikes a balance between the number of conditions considered and the severity of their impact.
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44 The two indices also included different numbers of long-term conditions (61 for the hospital discharge definition; 30
45 for the pharmaceutical dispensing definition). Including a higher number of conditions should generally increase the
46 recorded prevalence of multimorbidity, as there are more conditions that can be included in the definition: this was
47 not the case in the current study, however, due to the nature of the data sources. To be coded as having
48 multimorbidity based on the past hospital discharge data required at least one prior hospital admission in the past
49 five years (with two or more different long-term conditions recorded across these admissions); whereas to be coded
50 with multimorbidity based on the pharmaceutical dispensing data only required dispensings of medications for at
51 least two long-term conditions in the past year. Thus the definition based on past hospital discharge data sets a
52 higher threshold for defining multimorbidity, and identifies people with multimorbidity who are at higher risk of
53 subsequent poor health outcomes, as noted above.
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While a pharmaceutical dispensing definition sits closer to primary-care level definitions of multimorbidity, determination of long-term health conditions from pharmaceutical data is limited in that (a) some medications are used to treat different conditions, and (b) not all long-term health conditions might require or respond to pharmaceutical treatment. On top of this, cost-related factors that restrict the ability to access primary health care consultations and/or pay for prescriptions⁴² mean that pharmaceutical dispensing based definitions may underestimate the prevalence of multimorbidity in socioeconomically deprived groups. Conversely, the number and breadth of diagnoses recorded on hospital discharge records are dependent on several factors, including the primary reason for the admission, requirements for reporting of health conditions in specific jurisdictions, and the quality of recording of information both by attending medical staff and clinical coders.^{43 44}

Other studies comparing different designs or data sources for estimating prevalence of multimorbidity have reported higher prevalence when the denominator comprises those currently receiving care or medication, compared to when denominators are based on registered patients or the general population.^{3 35} Recent studies from Quebec and Australia have suggested a 10% to 15% higher prevalence (respectively) when using a denominator based on primary care attendees rather than a general population denominator;^{36 38} and another study suggested higher prevalence when using health survey methods compared to examining electronic health records.⁴⁵ A recent Australian study that linked survey data (for ages 45 plus) with routine pharmaceutical and hospitalisation data returned comparable prevalence estimates between survey and pharmaceutical data sources (37.4 and 36.1%), which were both around 17 percentage points higher than prevalence estimated using hospital data (19.3%).¹⁹

There are important equity considerations that arise from the patterning of multimorbidity by age, ethnicity, and socioeconomic status, especially considered in conjunction with this group's increased risk of subsequent hospital admission or death within the one-year follow-up period. The higher prevalence of multimorbidity in the Māori and Pacific populations also raises issues of equity in health outcomes: as such, interventions in NZ that aim to prevent multimorbidity or improve outcomes for those with multimorbidity need to consider the equity impacts of such interventions.⁴⁶ While these prevalence results are specific to NZ, we expect that patterning of multimorbidity by sociodemographic profile and the adjusted estimates for increased risk of poor health outcomes with multimorbidity should be generalizable to other countries.

Conclusions

Multimorbidity is common amongst NZ adults, with older people, Māori and Pacific ethnic groups and the socioeconomically disadvantaged having higher prevalence (on both of the measures used). Pharmaceutical dispensing data should give a better proxy for the prevalence of multimorbidity that could be determined from primary-care level data sources compared to using past hospital admission diagnosis data, although these estimates may be subject to bias arising from differential access to healthcare and pharmaceuticals between different population groups (e.g. by ethnic groups).

Looking more broadly at the health system, these results support calls to consider the existence of multimorbidity in the design of health services, which requires a continued shift from management of individual diseases to care of the whole patient.^{8 9 47} The impact of an aging population (and hence higher numbers of people with multimorbidity) combined with the substantial costs of providing health care for people with multimorbidity^{5 14 15} will also present a major challenge to the sustainability of health care systems. This has important implications for both planning health services to improve management for those who are already unwell, but perhaps more importantly for justifying appropriate targeting of interventions aimed at preventing long-term conditions.⁷

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1 Ethical approval was given by the University of Otago Human Ethics Committee (Health) at the start of the study
2 (HD14/29). A poster showing results looking at the prevalence of multimorbidity in NZ in 2012 was presented at the
3 World Congress of Epidemiology, Saitama, Japan, in August 2017.

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5 sort and count clinical conditions; and the Ministry of Health for supplying the data used in this study.

7 We would also like to acknowledge the input of our wider C3 research group and multimorbidity project team,
8 especially those clinicians who provided initial feedback on processes for identifying conditions.

10
11 **COMPETING INTERESTS**

12
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14
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16
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18
19 **AUTHOR CONTRIBUTIONS**

20
21 DS and JS conceived and obtained funding for the study.

22
23 JS designed and conducted the analyses, had full access to all of the data in this study and takes complete
24 responsibility for the integrity of the data and the accuracy of the data analysis.

25
26 DS, KS, and EM contributed to the interpretation of the results.

27
28 JS drafted the manuscript.

29
30 All authors revised the manuscript for publication and approved the final version.

31
32 **DATA SHARING**

33
34 Data for this study were provided by the New Zealand Ministry of Health (reference number: 2017-0609) following
35 ethical approval, and may be available to other researchers who meet data access requirements. Code for data
36 processing and analysis is available from the first author (JS) on request.
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FIGURE TITLES

Figure 1. Prevalence of multimorbidity (two or more conditions) by age group, according to hospital discharge diagnosis and pharmaceutical dispensing data sources

Figure 2. Prevalence of multimorbidity (two or more conditions) by age group and sex, according to hospital discharge diagnosis and pharmaceutical dispensing data sources

Figure 3. Prevalence of multimorbidity (two or more conditions) by age group and ethnicity, according to hospital discharge diagnosis and pharmaceutical dispensing data sources

Figure 4. Prevalence of multimorbidity (two or more conditions) by age group and NZDep quintile, according to hospital discharge diagnosis and pharmaceutical dispensing data sources

Figure 5. Age and sex standardised risk of mortality (left panel), ambulatory sensitive hospitalisation [ASH] admission (middle panel) and overnight non-maternity admission (right panel) within one year of index date, by multimorbidity status (defined based on hospital discharge diagnosis or pharmaceutical dispensing data)

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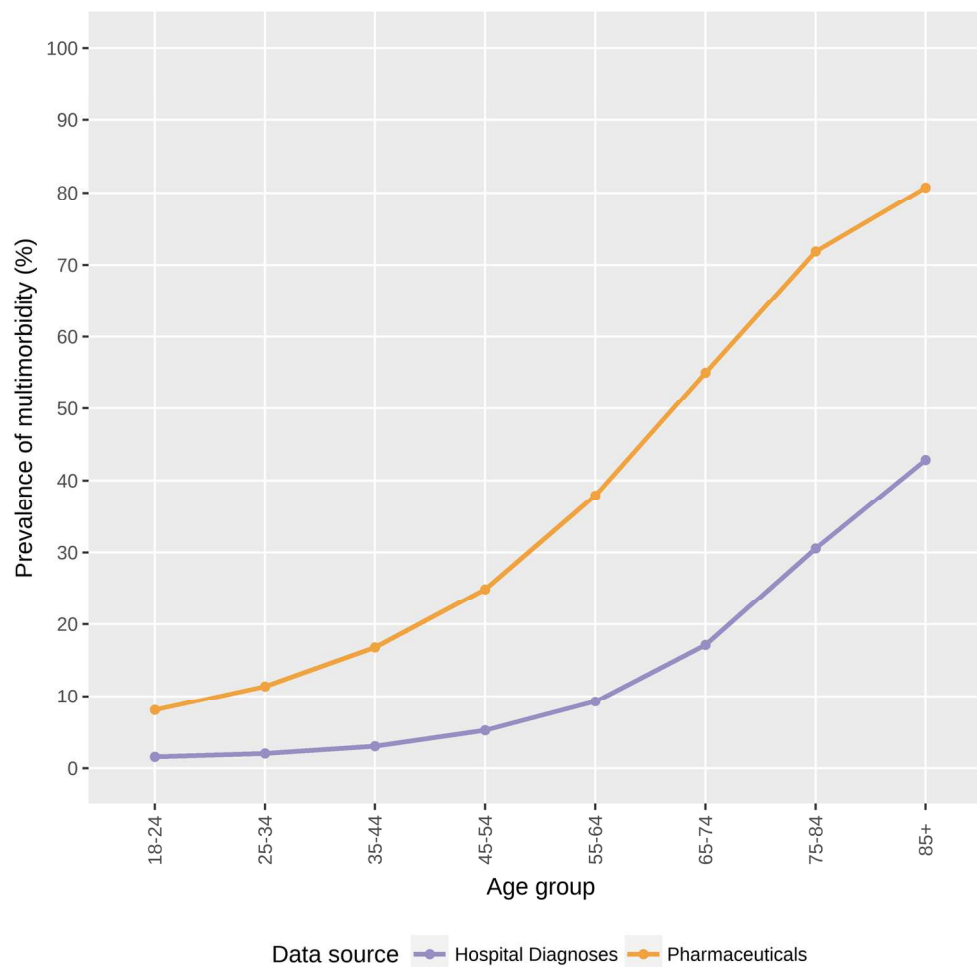


Figure 1: Prevalence of multimorbidity (two or more conditions) by age group, according to hospital discharge diagnosis and pharmaceutical dispensing data sources

152x152mm (300 x 300 DPI)

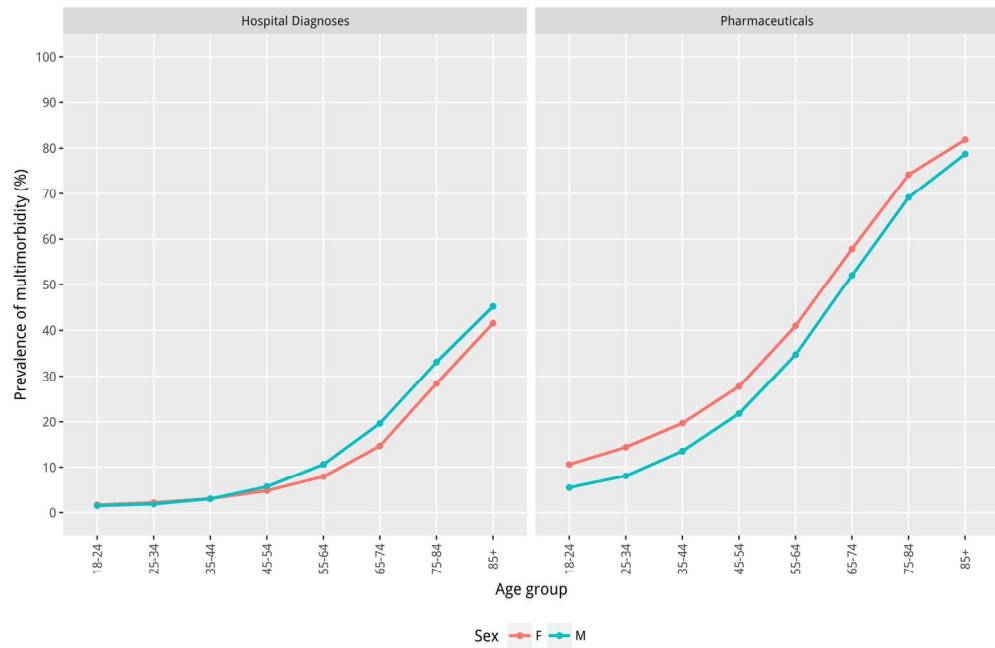


Figure 2: Prevalence of multimorbidity (two or more conditions) by age group and sex, according to hospital discharge diagnosis and pharmaceutical dispensing data sources

152x101mm (300 x 300 DPI)

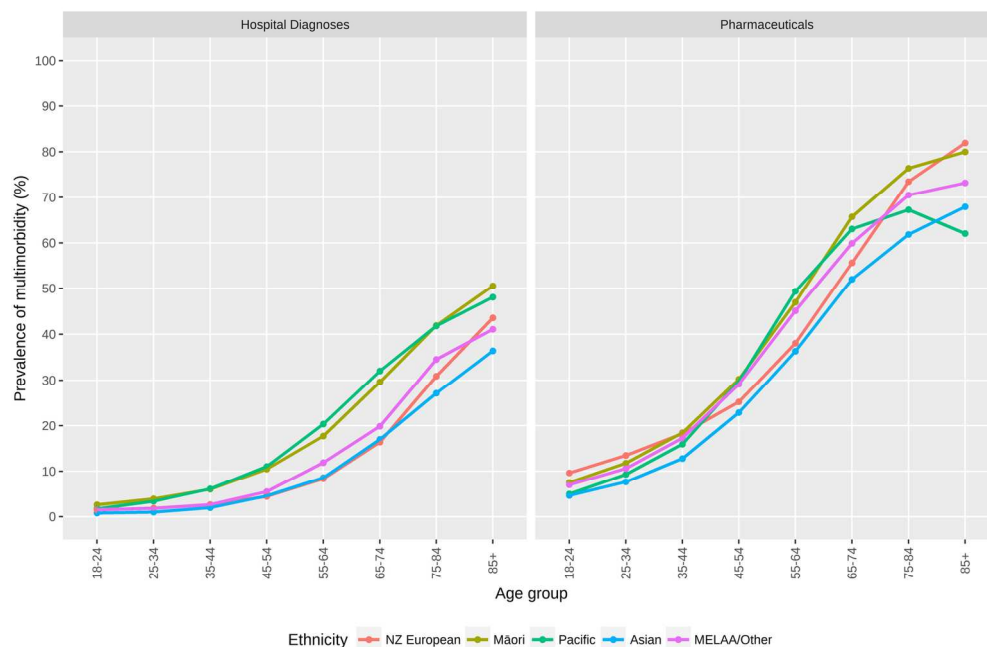


Figure 3: Prevalence of multimorbidity (two or more conditions) by age group and ethnicity, according to hospital discharge diagnosis and pharmaceutical dispensing data sources

152x101mm (300 x 300 DPI)

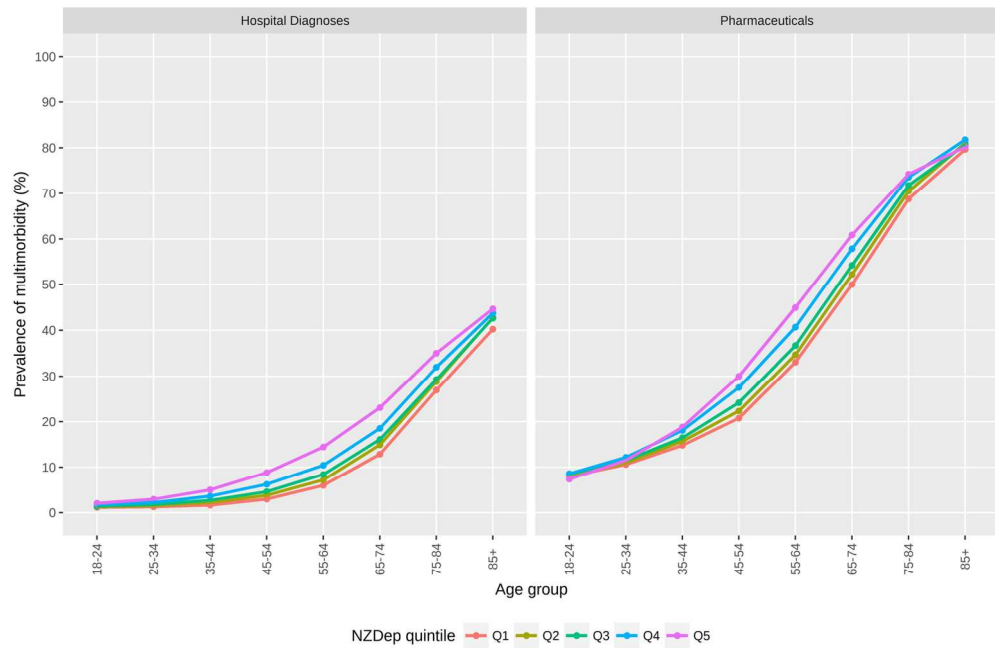


Figure 4: Prevalence of multimorbidity (two or more conditions) by age group and NZDep quintile, according to hospital discharge diagnosis and pharmaceutical dispensing data sources

152x101mm (300 x 300 DPI)

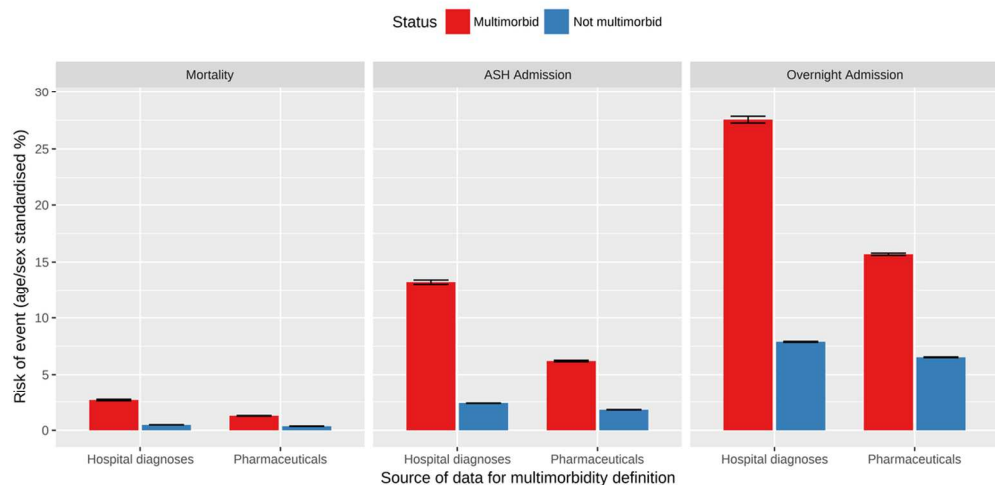


Figure 5: Age and sex standardised risk of mortality (left panel), ambulatory sensitive hospitalisation [ASH] admission (middle panel) and overnight non-maternity admission (right panel) within one year of index date, by multimorbidity status (defined based on hospital discharge diagnosis or pharmaceutical dispensing data)

114x57mm (300 x 300 DPI)

Supplementary Table A. Drug classes and medications included in the P3 index, with PHARMAC modified ATC codes and suggested ATC code classifications

[illegible]

1				<u>C01B</u>	<u>C01AA05</u>
2					C01BA01
3					C01BA02
4					C01BA03
5	Arrhythmias	Anti-arrhythmics	71301		C01BB01
6					C01BB02
7					C01BB03
8					C01BC03
9					C01BC04
10					C01BD01
11	Congestive heart failure (CHF)	Loop diuretics	73101	<u>C03CA</u>	C03CA01
12					C03CA02
13	Dementia	Donepezil, Rivastigmine	223201	<u>N06D</u>	N06DA02
14					N06DA03
15				<u>N06A</u>	N06AA01
16					N06AA02
17					N06AA04
18					N06AA06
19					N06AA09
20					N06AA10
21					N06AA10
22					N06AA12
23					N06AA16
24					N06AA17
25					N06AA21
26					N06AB03
27					N06AB03
28	Depression	Cyclic, MAOI, SSRI and other antidepressants	220501,220504,220505,220509,220507, 221001, 221002, 221007		N06AB04
29					N06AB05
30					N06AB06
31					N06AB06
32					N06AB10
33					N06AF03
34					N06AF04
35					N06AG02
36					N06AX03
37					N06AX06
38					N06AX11
39					N06AX11
40					N06AX16
41					N06AX16

1					<i>Insulin products</i>
2					<i>(prefix)</i>
3				<u>A10A</u>	A10A
4					<i>Other products:</i>
5				<u>A10B</u>	A10BA02
6					A10BB01
7					A10BB02
8					A10BB03
9	Diabetes	Insulin; oral hypoglycaemics; Insulin/glucose testing equipment****	11311,11301,11305,11307,11309,11303, 11312, 11507,11501,11509,11512, 11515,11504,420603		A10BB05
10					A10BB07
11					A10BB09
12					A10BF01
13					A10BG02
14					A10BG03
15					A16AB06
16				<u>H01BA</u>	H01BA02
17					<u>H04AA01</u>
18					<u>V03AH01</u>
19				<u>N03A</u>	N03AA02
20					N03AA03
21					N03AB02
22					N03AD01
23					N03AE01
24					N03AF01
25					N03AF02
26					N03AG01
27	Epilepsy	Anticonvulsants	220701, 220702, 220703		N03AG04
28					N03AX03
29					N03AX09
30					N03AX11
31					N03AX12
32					N03AX14
33					N03AX17
34					N03AX18
35					<u>N05BA09</u>
36					<u>N05CC05</u>

Gastric acid disorder	H2 blockers; proton pump inhibitors; other antiulcerants; antacids	10102, 10104, 11001, 11003, 11002, 11007, 11010, 11013	<u>A02A</u> <u>A02B</u>	A02AA05 A02AB01 A02AC01 A02AF02 A02BA01 A02BA02 A02BA03 A02BA04 A02BB01 A02BC01 A02BC02 A02BC03 A02BD01 A02BD05 A02BD08 A02BX01 A02BX02 A02BX03 A02BX05 A02BX12 A02BX13
Hepatitis B/C	Interferon/Ribavirin combinations	161905, 162201		<u>J05AF05</u> <u>J05AF08</u> <u>J05AF10</u> <u>L03AB04</u> <u>L03AB05</u> <u>L03AB10</u> <u>L03AB11</u> <u>L03AB60</u>

HIV	Anti-HIV antivirals	162001, 162003, 162005, 162103	<u>J05AE</u>	J05AE01 J05AE02 J05AE03 J05AE04 J05AE08 J05AE10 <u>J05AF01</u> <u>J05AF02</u> <u>J05AF03</u> <u>J05AF04</u> <u>J05AF05</u> <u>J05AF06</u> <u>J05AF09</u> J05AG01 J05AG03 J05AG04 J05AR10 <u>J05AR</u> <u>J05AX07</u>
Hypothyroidism	Thyroid agents	141401	<u>H03A</u>	H03AA01 H03AA02 H03AA03
Ischemic heart disease/Angina	Nitrates	73401	<u>C01DA</u>	C01DA02 C01DA52 C01DA05 C01DA08 C01DA58 C01DA14 <u>C01DX16</u>
Malnutrition	Enteral nutritional supplements****	420201, 420202, 420203, 420204, 420401, 420632, 420631, 420604, 420605		
Migraine	Antimigraine medications (acute and prophylactic)	221301, 221304	<u>N02C</u>	N02CA01 N02CA02 N02CA04 N02CC01 N02CC04 N02CX01 N02CX02
Multiple sclerosis	Multiple sclerosis treatments (B interferon; glatiramer)	222601, 222604		<u>L03AB07</u> <u>L03AB08</u> <u>L03AX13</u> <u>L04AA23</u> <u>L04AA27</u>

Osteoporosis/Paget's	Alendronate; Etidronate; Calcium supplementation	13801, 190802, 190804, 190806	<u>H05BA</u> <u>M05BA</u> <u>M05BB</u>	<u>A12AA</u> <u>G03XC01</u> <u>H05AA02</u> H05BA01 M05BA01 M05BA03 M05BA04 M05BA07 M05BA08 M05BB01 M05BB02 M05BB03 M05BB04 M05BB07 M05BB08 <u>V03AG01</u>
Pancreatic insufficiency	Pancreatic exocrine enzyme replacements	12201	<u>A05AA</u>	A05AA01 A05AA02 <u>A09AA02</u>
Parkinson's disease	Antiparkinsonian agents (dopamine agonists, specified anticholinergics)	221904, 221901, 220101	<u>N04</u>	<u>N01AX03</u> <u>N01BB01</u> N04AA02 N04BA01 N04BA01 N04BB01 N04BC01 N04BC02 N04BC04 N04BC04 N04BC05 N04BC05 N04BC07 N04BD01 N04BX01 N04BX02

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Psychotic illness	Antipsychotics (oral and depot)	222204, 222201, 222208	N05AA01 N05AA02 N05AB02 N05AB02 N05AB06 N05AC01 N05AC02 N05AC04 N05AD01 N05AD01 N05AD08 N05AE04 N05AF01 N05AF04 N05AF05 N05AG01 N05AG02 N05AH01 N05AH02 N05AH03 N05AH04 N05AL01 N05AL05 N05AN01 N05AX08 N05AX12 N05AX13
Pulmonary hypertension, PVD	Endothelin receptor antagonists; Phosphodiesterase Type 5 inhibitors; Prostacyclin analogues; vasodilators	74005, 74007, 74009, 74001	<u>C01DX16</u> <u>C02DB02</u> <u>C02DC01</u> <u>C02KX01</u> <u>C02KX02</u> <u>C04AC02</u> <u>C04AD03</u> <u>C04AX01</u> <u>V03AB22</u>

Reactive airway disease	Inhaled bronchodilators and corticosteroids; anticholinergic agents; mast cell stabilisers; Leukotriene inhibitors; respiratory devices	283001, 283010, 283401, 283410, 281001, 282404, 282402, 284001, 284302, 284502, 285302	<u>R03</u>	<u>C01CA26</u> <u>N06BC01</u> R03AB03 R03AC02 R03AC03 R03AC04 R03AC06 R03AC12 R03AC13 R03AC18 R03BA01 R03BA02 R03BA05 R03BB01 R03BC01 R03BC03 R03CC02 R03CC03 R03CC04 R03CC05 R03CC12 R03DA04 R03DA02 R03DA05
Rheumatoid arthritis	Antirheumatoid agents; TNF inhibitors	190701, 190702	<u>M01C</u>	<u>L04AA13</u> <u>L04AB01</u> M01CB01 M01CB03 M01CB04 M01CC01 <u>M02AB01</u>
Steroids-responsive conditions	Glucocorticoids (systemic corticosteroids)	140701	<u>H02AA</u> <u>H02AB</u>	<u>H01AA01</u> H02AA02 H02AB01 H02AB02 H02AB04 H02AB06 H02AB07 H02AB08 H02AB09 H02AB10

Transplant/ Auto-immune disorders	Immunosuppressants	250701, 250706		<u>L01XE10</u> <u>L04AA06</u> <u>L04AA10</u> <u>L04AD01</u> <u>L04AD02</u> <u>L04AX01</u>
Tuberculosis	Antitubercular agents	161601	<u>J04A</u>	<u>J01MA09</u> J04AA01 J04AB01 J04AB02 J04AB04 J04AB30 J04AC01 J04AD01 J04AD03 J04AK01 J04AK02 J04AM02 <u>J04BA01</u> <u>J04BA02</u>
CVD medication categories:				
Antiplatelet	Antiplatelet agents; coagulation check strips****	40701		<u>B01AB10</u> <u>B01AC04</u> <u>B01AC06</u> <u>B01AC07</u> <u>B01AC22</u> <u>B01AC24</u>
Hyperlipidaemia	Lipid lowering agents	41301, 41304, 41302, 41303, 41308, 73201, 73202, 73203, 73205, 73208	<u>C10AB</u> <u>C10AC</u>	C10AB01 C10AB02 C10AB04 C10AC01 C10AC02 <u>C10AD02</u> <u>C10AD06</u> <u>C10AD52</u> <u>C10AX02</u> <u>C10AX06</u> <u>C10AX09</u>

1			<u>C02A</u>	C02AB01
2				C02AB02
3				C02AC01
4			<u>C02C</u>	C02CA01
5				C02CA04
6				C02CC02
7			<u>C03A</u>	C03AA01
8				C03AA04
9				C03AA07
10				C03AA08
11				C03AB01
12			<u>C03B</u>	C03BA04
13				C03BA08
14				C03BA11
15			<u>C03D</u>	C03DA01
16				C03DB01
17				C03DB01
18				C03DB02
19			<u>C03EA</u>	C03EA13
20		Beta blockers; calcium channel blockers;		<u>C04AB01</u>
21	Ischemic heart	ACE inhibitors; Angiotensin II inhibitors;	70101, 70701, 70702, 70703, 71601,	<u>C04AX02</u>
22	disease/Hypertension	Thiazides; Potassium-sparing agents;	71901, 72201, 72202, 72801, 73107,	
23		combination antihypertensives; diuretics	73104, 73110, 70401, 70705	
24		and other hypertensives (Clonidine,		<u>C07AA01-08</u>
25		Hydralazine)		C07AA01
26				C07AA02
27				C07AA03
28				C07AA05
29				C07AA06
30				C07AA07
31				C07AA12
32			<u>C07AB02-08</u>	C07AB02
33				C07AB03
34				C07AB04
35				C07AB07
36				C07AB08
37			<u>C07AG</u>	C07AG01
38				C07AG02
39			<u>C08CA</u>	C08CA01
40				C08CA02
41				C08CA03
42				C08CA05
43				<u>C08DA01</u>
44				<u>C08DB01</u>
45				<u>C08EX02</u>
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			<u>C09AA</u>	C09AA01
				C09AA02
				C09AA03
				C09AA04
				C09AA06
				C09AA07
				C09AA08
				C09AA10
			<u>C09CA</u>	C09CA01
				C09CA06

* PHARMAC’s modified ATC codes, as available in the core data source and used in classification of indices.

** Suggested mapping to ATC code groups.

***Suggested specific ATC codes based on medications discovered in current NZ Pharmaceutical data for this analysis. Bolded/underlined items are single-code suggestions that do not fall under the groupings in the preceding column.

**** Some or all items coded in the PHARMAC-modified ATC coding system have no corresponding item in the WHO’s ATC coding system.

Supplementary Methods on Multiple Imputation

Sensitivity analysis (text reproduced from body of main paper)

To address the impact of missing covariate data (5.8% of individuals missing ethnicity and/or NZDep quintile), we used multiple imputation to examine whether the associations measured in the main analysis could have been biased due to exclusion of individuals with missing data (complete case analysis). Five imputation datasets were created using chained equations³² (using the mice package in R³³). These datasets imputed missing values for ethnicity and NZDep quintile (as polynomial variables) based on all other variables in the analytical model including exposure variables and outcome variables (multimorbidity status, age group, sex, ethnicity, NZDep quintile, and all outcome variables). The imputation models also included auxiliary information on each person's District Health Board of residence (the 20 administrative divisions of the public health system in NZ, which provides additional information on sub-national distribution of people by ethnicity and socioeconomic deprivation). Further details on this analysis and underlying assumptions are given with Supplementary Table B.

References from main paper:

32. White IR, Royston P, Wood AM. Multiple imputation using chained equations: Issues and guidance for practice. *Stat Med* 2011;30(4):377-99. doi: 10.1002/sim.4067 [published Online First: 2011/01/13]
33. van Buuren S, Groothuis-Oudshoorn K. mice: Multivariate Imputation by Chained Equations in R. *Journal of statistical software* 2011;45(3):1-67.

Supplementary Methods on Assumptions of Multiple Imputation

The following notes assume some familiarity with methods for missing data and multiple imputation: several overview papers have been previously published on this methodology¹⁻³.

In order for multiple imputation of covariates to be valid and useful, a key assumption is that data are missing at random (MAR), which means that the to-be-imputed values can be considered to be missing at random conditional on the variables included in the imputation model.^{1,2} Thus, an imputation process that draws on these conditioning variables (including exposure and outcome variables) to produce imputed values should be able to recover some information to account for the potential profile of those people who are missing some data. It is not possible to determine from a dataset whether data are missing at random or missing not at random (MNAR: i.e. some additional unmeasured information influences whether data are missing).^{2,3} However, including a sufficient number of meaningful variables as predictors in the imputation model process, including exposure and outcome variables, serves to make the missing at random assumption more plausible for a given scenario^{1,3}.

In the current study, we believe on theoretical grounds that the missing data (for ethnicity and socioeconomic status as measured by area of residence using NZDep 2013) are effectively missing at random, conditional on the variables included in our imputation model.

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Firstly, we assume that ethnicity data collected in the routine data sources is more likely to be present for people with multiple health contacts (because these are opportunities to collect ethnicity data in line with NZ's ethnicity data protocols). The imputation models explicitly include information on multimorbidity status and subsequent health outcomes in the imputation process. This means health-status is being used as part of the imputation process, which should lead to valid results for the imputation analysis (in conjunction with other known sources of patterning for ethnicity across NZ, including geographic variation and variation of socioeconomic status by ethnicity).

Secondly, NZDep values (the second missing variable in the regression models) tend to be missing when address information for a given person is either unavailable or incompletely recorded in the Ministry of Health's master databases (and hence geocoding cannot be performed to assign that person with an area-based code), or when there an otherwise-correct address cannot be mapped to the area codes recorded in the measure NZDep. The chances of this second scenario depend upon the discrepancy between the time at which a person's address is measured (usually the most recent update to their health record) and the timing of the specific five-yearly census from which the NZDep measure was derived (in this case, the 2013 census conducted in March 2013).

Supplementary Table B below includes both the complete-cases results of the regression models (top half, reproducing results from Table 4 of the main paper) and also the results of the analysis of the multiply-imputed datasets (bottom half of Sup. Table B) following the analytical procedures given in the main paper (as reproduced above). As can be seen, and as reported in the main paper, the results are almost identical in the two analyses: point estimates are marginally higher in the imputed-data results, but not substantively different.

References for Supplementary Methods text:

1. Donders AR, van der Heijden GJ, Stijnen T, et al. Review: a gentle introduction to imputation of missing values. *J Clin Epidemiol* 2006;59(10):1087-91. doi: 10.1016/j.jclinepi.2006.01.014 [published Online First: 2006/09/19]
2. Sterne JA, White IR, Carlin JB, et al. Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. *BMJ* 2009;338:b2393. doi: 10.1136/bmj.b2393 [published Online First: 2009/07/01]
3. Harel O, Zhou XH. Multiple imputation: review of theory, implementation and software. *Stat Med* 2007;26(16):3057-77. doi: 10.1002/sim.2787

Supplementary Table B. Results from original complete-case analysis (top panel, Table 4 from main paper) and from analysis of multiply imputed data (n=5 imputation datasets).

Model†	Odds ratio (95% CI) for risk of outcome with multimorbidity*					
	Hospital discharge definition			Pharmaceutical dispensing definition		
	Mortality	ASH‡	Admission§	Mortality	ASH‡	Admission§
COMPLETE CASE ANALYSIS						
Unadjusted model	17.6 (17.2, 18.1)	8.4 (8.3, 8.5)	5.6 (5.6, 5.7)	14.7 (14.2, 15.2)	5.5 (5.5, 5.6)	3.7 (3.7, 3.7)
Adjusted age, sex	4.8 (4.7, 5.0)	4.9 (4.9, 5.0)	3.6 (3.5, 3.6)	4.0 (3.9, 4.2)	3.6 (3.6, 3.7)	2.6 (2.6, 2.7)
+ adjust ethnicity	4.7 (4.6, 4.8)	4.7 (4.6, 4.7)	3.5 (3.5, 3.5)	3.9 (3.8, 4.1)	3.6 (3.5, 3.6)	2.6 (2.6, 2.6)
+ adjust NZDep quintile	4.6 (4.5, 4.7)	4.6 (4.5, 4.6)	3.5 (3.4, 3.5)	3.9 (3.7, 4.0)	3.5 (3.5, 3.6)	2.6 (2.6, 2.6)
MULTIPLE IMPUTATION ANALYSIS						
Unadjusted model	18.0 (17.5, 18.4)	8.7 (8.6, 8.9)	5.8 (5.8, 5.9)	14.8 (14.3, 15.3)	5.7 (5.6, 5.8)	3.8 (3.8, 3.8)
Adjusted age, sex	4.9 (4.8, 5.0)	5.1 (5.1, 5.2)	3.7 (3.7, 3.7)	4.1 (4.0, 4.2)	3.7 (3.7, 3.8)	2.7 (2.7, 2.7)
+ adjust ethnicity	4.8 (4.6, 4.9)	4.8 (4.8, 4.9)	3.6 (3.6, 3.7)	4.0 (3.9, 4.1)	3.7 (3.6, 3.7)	2.7 (2.7, 2.7)
+ adjust NZDep quintile	4.7 (4.6, 4.8)	4.7 (4.7, 4.8)	3.6 (3.6, 3.6)	3.9 (3.8, 4.1)	3.6 (3.6, 3.7)	2.7 (2.6, 2.7)

* Reference group is individuals without multimorbidity (i.e. either zero or only one long-term conditions identified)

† All models run on complete-case data only (n=3,288,646; total of n=201,101 missing ethnicity &/or NZDep)

‡ Ambulatory sensitive hospitalisation (ASH)

§ Non-maternity admissions with at least an overnight stay.

Note: Complete-cases analysis reproduces results shown in Table 4 of main paper (regression results for people with complete data for all covariates included in the fully-adjusted model). 5.8% of individuals were missing ethnicity and/or NZDep quintile data in the complete-case analysis.

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page # / note
Title and abstract	1	(a) Indicate the study’s design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4-5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(a) Cohort study—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5
		Case-control study—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls	
		Cross-sectional study—Give the eligibility criteria, and the sources and methods of selection of participants	
		(b) Cohort study—For matched studies, give matching criteria and number of exposed and unexposed	
		Case-control study—For matched studies, give matching criteria and the number of controls per case	n/a
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5
Bias	9	Describe any efforts to address potential sources of bias	(discussion)
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	6-7
		(b) Describe any methods used to examine subgroups and interactions	n/a
		(c) Explain how missing data were addressed	p.6
		(d) Cohort study—If applicable, explain how loss to follow-up was addressed	n/a
		Case-control study—If applicable, explain how matching of cases and controls was addressed	
		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	p. 7 (imputation)

Results

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	n/a (cross-sectional)
		(c) Consider use of a flow diagram	Not included (one-step selection)
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	
		(b) Indicate number of participants with missing data for each variable of interest	Table 1, Table 4 (footnotes to each)
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	P6. For prospective element
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	p. 8, Table 3
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	n/a
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	n/a
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	p. 7-11, all tables and figures.
		(b) Report category boundaries when continuous variables were categorized	Table 1, Figs 1-4
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Absolute risk on p. 7-11, Table 4
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	p. 11, Supp. Table B

Discussion

Key results	18	Summarise key results with reference to study objectives	p. 14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	p. 14-15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	p. 14-16
Generalisability	21	Discuss the generalisability (external validity) of the study results	p. 16

Other information

Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	p3 and online statement
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*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.